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DIVERTICULITIS AND CARCINOMA OF THE SIGMOID

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DIVERTICULITIS of the sigmoid is usually readily diagnosed from the symptoms, physical examination, laboratory studies, and characteristic x-ray findings. Complications which may arise, such as abscess, perforation, peritonitis, obstruction, or fistula tend to obscure the clear-cut picture and may render it quite confusing if accompanied by bleeding.

Cancer of the sigmoid, likewise, gives a reasonable pattern by which its recognition can be made by most clinicians. The laboratory tests for blood in the stools; sigmoidoscopic observation and biopsy; and the study of barium enemas with contrast air injections lead to a conclusive diagnosis in most instances.

When cancer of the sigmoid becomes complicated by growing through the intestinal wall, abscess may follow it. Peritonitis with adhesions between the omentum, small intestine, and bladder, makes pictures similar to complicated diverticulitis. In women, adhesions to the tubes and ovaries add to the difficulties of gynecologic diagnosis. Rarely fistulas develop between the colon, bladder, and small intestine. Obstructions may be partial or complete. And finally, inflammation in the cancerous area may cause fever, leukocytosis, and a tender fixed mass almost exactly comparable to an acute diverticulitis.

The attempts to arrive at a correct diagnosis involve all the acumen of experienced clinicians. The radiologist usually gives considerable assistance. If he can show the area of the sigmoid in spasm, irritable, distensible, and tender, with a few diverticula, the evidence is presumptive that diverticulitis is the answer. The spasm often extends well above the irritable zone and there is no evidence of chronic distention of the large intestine above the area. If, on the other hand, the segment is short, the area shows poor filling, is nonsensitive, rigid, firm, and not distensible, with evidence of chronic distention above it, the likelihood of cancer is strong.

In complicated diverticulitis and in inflammatory carcinomas all these signs may fail. The barium cannot be retained and none can be made to pass beyond

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the rectosigmoid junction in many instances. No diverticula can be demonstrated and the nodular appearance of cancer cannot be shown. All that the radiologist can say under such circumstances is that there is an obstruction at the rectosigmoid junction the nature of which he cannot determine. Occasionally, a small quantity of barium may pass the spasm or obstruction area giving imperfect filling of the sigmoid. Flecks of barium may be interpreted as diverticula when they really represent ulcerations in a carcinoma. Or the imperfect filling may simulate the filling defects of neoplasm when due to spasm alone.

The diagnosis in the final analysis depends upon the microscopic picture. It would seem relatively simple to procure a biopsy specimen through the sigmoidoscope or at exploratory operation. But it is surprising how difficult it is to get a satisfactory sigmoidoscopic examination—and dangerous as well. The specimens taken at exploration which appear certain to be positive for cancer many times turn out to be inflammatory; and the enlarged lymph nodes prove to be hyperplasia. Repeated biopsies have failed in some instances to give the true answer because the cancer is walled off by dense inflammatory reaction and is not accessible.

It is well to remember that a negative report for carcinoma, however, does not mean that there is surely none present. From the gross specimen it is usually possible to determine whether the lesion is benign or malignant by opening the bowel and examining the mucosa. On rare occasions there may be an infiltrating carcinoma which is of the linitis plastica type and the mucosa is thought to represent an ulcerative colitis. Such cases are confusing and puzzling. We had one such in our series.

The coexistence of diverticulosis or diverticulitis and cancer in the sigmoid colon is considered quite rare. Oren reported on 2 such cases in 102 cases of diverticulosis. He quoted the other writers noted here. Fallon had only 3 cancers in 625 cases of diverticulitis and in 1,800 cases of diverticulosis. In 1,600 operations for cancer of the colon only 19 had diverticula in the same area. Rankin and Brown found cancer in only 4 of 227 cases of diverticulitis and in all their cancer operations diverticula were present in only 4. Jones reported the two lesions together in 3 of 300 cases. Arnheim reviewed the diverticulitis cases admitted to the Mount Sinai Hospital in a 10 year period. There were 35 cases. In only 1 case was there an associated carcinoma.

There is no evidence that diverticulitis is a precursor of cancer. The fact that the two lesions may coexist is easily accounted for. According to Karsner, diverticulosis of the large intestine is present in 25 to 30 per cent of all adults. The sigmoid is the segment of predilection for this condition. It is generally conceded that 25 per cent of all the colon cancers occur in the sigmoid. The probability of the two conditions existing together is therefore to be expected.

When the diagnosis is in doubt it is fair to give a reasonable medical trial in the hope that the inflammation may subside. The usual rest in bed, low residue diet, antispasmodics, and antibiotics are employed. The fever, leukocytosis, and tenderness should subside in a few days. Inflammatory masses should get smaller. In case the inflammation does subside attempts to make an accurate diagnosis should be pushed, especially if bleeding is present. This latter

is a dangerous symptom which demands careful attention. Continued bleeding calls for exploratory operation. Surgery should be as radical as for cancer taking parts of adherent organs with the mass and repairing the defects afterward. These operations are by no means simple. Sometimes two or three loops of small intestine and a portion of the urinary bladder will be involved in the mass. To separate them will be fatal if there is cancer spreading through these tissues. Consequently in some cases tissues will be removed for inflammation only but this is a risk that must be balanced against that of scattering the cells of a possible cancer.

Eighteen cases of coexistence of diverticulitis and carcinoma of the sigmoid segment have been studied in the University of Rochester Hospitals during the past twenty years. A similar number of acute complicated diverticulitis cases have been proved not be associated with cancer only after radical resection and microscopic examination. Abstracts of the first group are appended here. Abstracts of some of the more interesting of the second group are also included. There have been patients who have had complications of diverticulitis who have also had carcinomas elsewhere in the large intestine as at the cecum, hepatic flexure, transverse colon, splenic flexure, and rectum. These cases are not included.

CASES OF COEXISTENCE OF DIVERTICULITIS AND CARCINOMA

CASE 1 (84887).—J. K., a 50-year-old man, was admitted to the Rochester Municipal Hospital on Aug. 18, 1938. For seven months, he had had a bloated feeling in the lower abdomen. Pain was present in the morning, and was relieved by belching and soda. It got progressively worse. The stools had become smaller in diameter during the preceding few months, and loose in character because he took cathartics. Three weeks previously, he had noticed considerable bright red blood in the stool and again three days prior to admission. Pain in the lower abdomen became worse. He lost about ten pounds. He had had hemorrhoids for years.

At the time of entry his temperature was 39.5° C., pulse 110. He appeared chronically ill and complained of abdominal pain. There was distention in the lower abdomen and exquisite tenderness in both lower quadrants, more marked on the left.

Blood studies showed no anemia. A barium enema had been done two days previously and it showed marked spasm and tenderness in the sigmoid. There was a ragged, somewhat narrowed area at the junction of the rectosigmoid below the spastic area. This could be either diverticulitis or carcinoma.

Diagnosis was made of a pelvic peritonitis due to perforation of the large bowel. At operation on Aug. 20, 1938, several abscess pockets were exposed and drainage instituted. No definite perforation was visualized. A cecostomy was done through a separate incision. Culture showed *Streptococcus viridans*. Prontylin was given. The left abdominal incision became infected with *Staphylococcus albus* and he had a severe hemorrhage from the abscess cavity. He went into shock and never rallied. He died on Sept. 2, 1938.

At pathology examination, there was a perforated diverticulum with generalized peritonitis. A carcinoma of the sigmoid was present also with metastases into the regional lymph nodes, into the liver, the pancreas, and both lungs.

CASE 2 (66474).—C. D., a 58-year-old woman, was admitted to Rochester Municipal Hospital on May 25, 1940.

One year and a half previously she had had abdominal pain occurring at the time she moved her bowels. The pain was crampy in nature and located chiefly in the left lower abdomen. The stools were sometimes streaked with blood. No change in the caliber of the stools was noted and there were no chills, fever, or urinary symptoms.

Four months previously the pain had become severe and a dragging sensation remained in the lower abdomen. Frequency and dysuria had been added to her other complaints. A mass to the right of the umbilicus was observed on March 7, 1940.

She was well nourished and lying quietly though she complained of severe pain. In the right lower quadrant there was a large, tender, sausage-shaped mass.

She was not anemic though the stools showed 2+ guaiac.

A barium enema showed diverticula of the sigmoid with two areas which might represent filling defects. Carcinoma could not be excluded.

She ran a fever on the third day after admission and it continued a course indicative of sepsis for 1 week. The mass in the right lower quadrant became larger and acutely tender.

On the tenth day after admission a pelvic abscess was drained. She did not do well for nearly four weeks. Then her temperature became normal, though she drained from the sinus and a mass was palpable still. After being afebrile for two and one-half weeks, she was discharged with a diagnosis of diverticulitis of the sigmoid with perforation and pelvic peritonitis, localized.

The pelvic abscess was drained again on Sept. 25, 1940, and she was discharged, afebrile, in six days.

Sigmoidoscopy was done on Jan. 1, 1941. The scope was inserted for 18 cm. Biopsy showed only acute and chronic inflammation.

She was explored on March 1, 1941. The sigmoid entered a large mass of tissue in front of the sacrum and was attached to the posterior body of the uterus. A colostomy was done. Tissue taken for biopsy showed acute and chronic inflammation. She did not make a rapid recovery but continued to run a fever and to have bouts of pain in the epigastrium and in the pelvis. It was decided to explore the distal loop through the colostomy. This was done on April 18, 1941, and carcinoma was diagnosed from biopsy specimens removed from a polypoid mass within the sigmoid loop. Acute and chronic inflammation was also present.

The family decided to take care of her at home. She was attended there by her local physician. She died on June 17, 1941.

CASE 3 (166696).—C. M., a 45-year-old man, was admitted to the Strong Memorial Hospital on July 12, 1940.

He had become progressively constipated during the preceding one and one-half years. The caliber of the stools became smaller so that at the time of admission they were lead-pencil-sized. There had been marked tenesmus with three to four small movements daily. Also, much distress after meals and vomiting on several occasions. Eight months previously, he had begun to pass tarry stools on the average of once a month. He had noted bright blood on the toilet paper also, but attributed this to a bleeding hemorrhoid which he had had for three years. He had become weak and easily tired. He had lost twenty-four pounds in the month before admission. A dull pain persisted in the right inguinal area and seemed to go through to the right hip.

He appeared to be chronically ill. His abdomen was distended throughout. There was tenderness over a smooth firm mass which could scarcely be palpated in the left inguinal region. Rectal examination showed an inflamed tender hemorrhoid and benign prostatic hypertrophy.

He did not have an anemia. His white blood count was 9,900. Stools were guaiac negative. Barium enema showed obstruction at the sigmoid. Proctoscopic examination revealed an obstructing mass.

Exploration showed the lower sigmoid and rectum to be incorporated in a mass of tissue adherent to the right side of the pelvis. It was firm and boggy. No evidence of metastatic carcinoma was found anywhere. In separating the loops with a finger there appeared, in the depths of the pelvis, a thick creamy pus. The question of diverticulitis or cancer was debated without a decision being reached. No tissue like carcinoma could be uncovered. A loop colostomy was done. Lymph nodes removed showed hyperplasia on microscopic examination.

Proctoscopic examination on July 31, 1940, showed no evidence of carcinoma for a distance of 16 cm. The rectum was slightly reddened and edematous high up. Barium introduced through the distal colostomy showed an irritable bowel and a questionable filling defect at the rectosigmoid. The film was not positive enough to make a differential diagnosis between inflammation and tumor.

He was discharged on Aug. 9, 1940. He had gained rapidly and felt much improved. He gained twenty pounds at home. The colostomy functioned well. Sigmoidoscopic examination on Oct. 21, 1940, was again inconclusive from below and through the distal colostomy. Barium study by the latter route showed a defect 2 to 3 inches long with irregular margins and ragged filling at the rectosigmoid junction. No diverticula could be identified, although one shadow was suggestive. The radiologist could not make a definite diagnosis, though he inclined toward malignancy because of the irregularity of the wall, the narrowing of the lumen, and the fixity of the area.

The patient was readmitted on Nov. 20, 1940, for further operation. He had done very well at home. At operation a tumor mass was found, involving the rectosigmoid. It was adherent to the base of the bladder. Resection was done and an end-to-end anastomosis made. Previous to this, three nodes were sent to the laboratory for frozen section. They showed no tumor.

The specimen was opened in the pathology laboratory. It showed multiple polyps with an ulceration at the lower portion of the sigmoid. Microscopic sections showed carcinoma with acute and chronic inflammation.

He was discharged on Dec. 5, 1940, in good condition. An abscess developed and was drained. In October, 1944, he showed carcinoma metastasis in the lung, and bronchopneumonia. There were metastases into the lymph nodes of the right thigh and pelvis and an anemia. After a long illness he died at home on March 16, 1946.

CASE 4 (10658).—E. M., a 53-year-old woman, was admitted to the Strong Memorial Hospital on Dec. 13, 1942.

Three days previously she had developed pain in the left lower quadrant, crampy in nature and radiating toward the symphysis. The pain increased in severity till the time of her admission. She got relief by lying on her back and on the right side. For three weeks she had had increasing constipation with tarry stools in the last three days. There were no bowel movements for two days. There had been no free blood nor change in the caliber of the stools. Some pain has been present on starting urination.

She was acutely ill with a temperature of 39.4° C., and pulse 108. There was a tender mass in the left lower quadrant extending from the symphysis along Poupart's ligament almost to the anterior superior spine. It moved with the uterus and there was marked tenderness on the left on pelvic examination. Rectal examination did not contribute anything significant.

The white blood count was 17,000. Barium enema studies showed a mass extrinsic to the colon but kinking the sigmoid. Two examinations failed to show diverticula. She was put on sulfathiazole, but after ten days could not tolerate it further. It was discontinued because of nausea. The mass rapidly decreased to one-third of its original size, her fever and leukocytosis subsided. She was discharged to be followed in the outpatient department. The diagnosis was ruptured diverticulum with abscess or perforation of cancer of the sigmoid.

She was readmitted in April, 1943. She had continued to lose weight. The mass was present still, fixed, and slightly tender.

A barium enema showed narrowing of the mid-sigmoid but with no sharp cutoff. There were two small diverticula present.

Operation under continuous spinal anesthesia showed a large mass filling almost the whole pelvis. There were many peritoneal implants of carcinoma. Biopsy showed an anaplastic type of carcinoma. Permanent colostomy was done for palliation.

She was discharged on May 4, 1943. She died at home on Oct. 5, 1943.

CASE 5 (61422).—C. L., a 60-year-old man, was admitted to the Strong Memorial Hospital on Sept. 11, 1942. He was known to have diverticula in the sigmoid from previous studies. Two weeks before admission he had crampy pain in the left lower quadrant with nausea but no vomiting. His bowel movements were soft and contained no blood.

He was well nourished and well developed. In the left lower quadrant there was slight spasm and on deep palpation a small tender firm mass was palpable.

The red blood count was 4.6 million, hemoglobin 14.5 Gm., white blood count 12,700. Stools showed a trace of occult blood. Barium enema showed diverticula of the sigmoid colon and a narrowing of the lumen.

Under conservative treatment he became better. The white blood count dropped to 9,000, but he worried because there had been so much cancer in his family history. His mother had died of cancer of the ovary, his father had died of cancer of the large intestine, and a sister had died of cancer of the breast. He asked for exploration which was done. The gross lesion appeared to be inflammatory but it was hard. A resection and an end-to-end anastomosis was done. Microscopic study showed cancer of the bowel as well as inflammation. He developed postoperative pneumonia but responded to sulfa drugs and was discharged in good condition.

He began to do poorly at home. Blood appeared in the stools and no source could be found by study. He received transfusions without benefit. An abscess finally developed in the region of the resection and a fecal fistula resulted. Another resection was performed but he continued to respond poorly. He died with metastases in the liver, two years after the first operation.

CASE 6 (99179).—F. M., a 62-year-old man was admitted to the Strong Memorial Hospital on Jan. 2, 1945.

He had had progressive increase in the number of his bowel movements over the preceding five weeks. The stools had become more watery and smaller in diameter. Dark specks of blood were present early in the course of this diarrhea and at times there were tarry stools also. Solid stools were pencil-thin or ribbonlike. There was localized lower abdominal pain and acute onset of severe burning on urination. He had lost ten to fifteen pounds in weight.

He was very deaf but did not appear acutely or chronically ill. He was obese. There was a visible and palpable mass in the right upper quadrant—probably liver. There was tenderness in the suprapubic area. The prostate was hard and fixed, nodular, and enlarged. Rectal examination was painful.

The red blood count was 4.8 million, hemoglobin 13.7, white blood count 9,700.

The urine showed 50 to 100 red blood cells to the high power field. The urine was infected with *Escherichia coli.*

The stool was pencil-like but contained no blood on chemical test.

Barium enema showed a filling defect at the rectosigmoid junction associated with numerous diverticula. It was considered to be a diverticulitis and not due to carcinoma, although the latter could not be ruled out definitely.

Sigmoidoscopic examination showed a hemorrhagic area in the sigmoid but the biopsied specimen was lost.

He was explored on Jan. 16, 1945. There was a large mass in the pelvis bound down by many adhesions. There were no signs of metastasis in the nodes or liver. A transverse, defunctioning colostomy was done.

He was discharged on Feb. 4, 1945, with a diagnosis of diverticulitis of the sigmoid, cystitis, and beginning or healing fistula to the bladder. The urologists considered that the prostate was enlarged but that the mass was above it in the region of the base of the bladder.

He was unable to gain weight at home. He had had frequency, nocturia, and foul, fecal-smelling urine. He had had chills and fever also. He drained pus and blood from his rectum, and this drainage increased during urination.

He was readmitted to the hospital on June 1, 1945. A large mass above the prostate was biopsied through the proctoscope. It showed carcinoma of the bowel on microscopic examination.

A cystostomy was performed on June 9, 1945.

He went downhill gradually and died on July 22, 1945.

Examination after death showed carcinoma of the sigmoid with extension through the posterior wall of the urinary bladder. There were other malignant polyps in the colon and mild cirrhosis of the liver. Benign prostatic hypertrophy was present.

CASE 7 (234407).—A. K., a 73-year-old woman, was admitted to the Strong Memorial Hospital on July 8, 1945. In September, 1944, she had noticed blood in her stools. She went to the hospital, had x-rays taken, and was put on a diet. Her bowels continued to be irregular but she passed more blood. She gained one and one-half pounds under treatment. Diagnosis of diverticulitis was made. Another x-ray series in April, 1945 showed obstruction of the large bowel. She had had diarrheal stools, about 10 to 20 per day. She had lost fifteen pounds since September, 1944.

She was alert and did not appear ill. She weighed ninety-seven pounds. In the left lower quadrant there was a freely movable, hard mass. Barium enema showed a filling defect at the rectosigmoid junction. There was also spasm of the sigmoid colon and numerous diverticula.

There were many diverticula in the sigmoid region and a mass the size of a tennis ball at the rectosigmoid at operation on July 13, 1945. The lesion was excised and an end-to-end anastomosis performed low down in the pelvis.

The pathology examination showed a carcinoma of the sigmoid with metastases to the regional nodes. Many small diverticula were present.

She made a good recovery. She gained twenty-three pounds by Nov. 14, 1945, and by Aug. 16, 1946, had reached one hundred and thirty-two pounds in weight. Her bowels gave no trouble. Examination showed no recurrence or metastases.

In January, 1947, she had left sciatic pain, knifelike, shooting from left buttocks to left popliteal space. Relief was obtained by opiates. X-rays of lumbar spine and femur in June, 1947, showed a compression type of lesion of a lumbar vertebra. She had lost eight pounds.

Three hard masses were present in the pelvis and there was involvement of the lumbar plexus. Relief was obtained by injection of the sciatic nerve with Eucupin in December, 1947.

She died at home in Jan. 1948. No autopsy was obtained.

CASE 8 (202569).—R. R., a 50-year-old woman, was admitted to Strong Memorial Hospital on Sept. 5, 1945. She had developed a persistent diarrhea nine months previous. She passed seven or more loose stools every morning and a similar number every night at bedtime. For five months the stools had contained blood and pus. She did not improve under conservative treatment. She was sent to a hospital and a proctoscopic examination showed cancer, proved by microscopic section. Barium enema could not be tolerated. She was discharged from the hospital at her request and entered the Strong Memorial Hospital. Her appetite had been good but she was no longer desirous of food. There was a continuous dull ache in the rectum.

She was obese and excitable. Nothing remarkable was found on physical examination. The red blood count was 5.2 million, hemoglobin 12.0, white blood count 17,000. The stools were guaiac negative. The white blood count rose to 20,000 and remained high for three to four days.

At operation on Sept. 10, 1945, an abscess was encountered in the cul-de-sac around the sigmoid. Thick pus was aspirated. There was a mass in the lower sigmoid extending through the rectal wall posteriorly and retroperitoneally into the upper part of the pelvis. The rectum was cut across low down and the lesion removed in toto. A permanent colostomy was made and the rectal remnant used to drain the pelvic area.

The pathologic specimen consisted of a 25 cm. segment of sigmoid and upper rectum. There was a necrotic carcinomatous ulcer 1.5 cm. in diameter with a perforation at a distance of 6 cm. from the distal end of the bowel. A firm mass of hard tissue infiltrated the

mesentery and epiploic fat. No lymph nodes were identified but seven large diverticula were present and there were two polypoid structures adjacent to the ulcer. Microscopic examination showed carcinoma.

She was discharged three weeks after operation in good condition.

She was readmitted on June 4, 1948, for a poorly functioning colostomy. It had narrowed down considerably. There was a hard irregular stony mass in the right side of the pelvis. The peritoneal cavity was full of fluid. The colostomy was revised. Metastatic and recurrent carcinoma were present. Her last note was recorded in October 1948.

CASE 9 (256333).—B. S., a 64-year-old woman, was admitted to Strong Memorial Hospital on Nov. 20, 1946.

For almost a year she had noted bright red blood in her stools daily, sometimes as much as a tablespoonful. There had been a slight decrease in the caliber of the stools over the summer. Her local physician gave her mineral oil which resulted in two to three small movements every morning. There had been an excellent appetite and she had gained ten to fifteen pounds over the past year.

Examination showed a markedly obese woman—over two hundred pounds in weight. Nothing abnormal could be found on physical examination.

The red blood count was 4.7 million, hemoglobin 16.8 Gm., white blood count 6,750.

Barium enema revealed numerous diverticula of the sigmoid. There was a slight narrowing of the mid-portion of the rectum, strongly suggesting an annular constriction.

At operation on Nov. 21, 1946, abdominal exploration was negative for metastatic carcinoma. The mid-portion of the sigmoid contained a freely movable, hard, indurated mass about 4 cm. in diameter. It was interpreted as diverticulitis. The bowel was transected above this and the mesentery divided down to the root. The bowel was transected below the sigmoid and this segment removed with the lesion described above. The distal bowel was covered with a rubber glove and the pelvic floor reconstituted above it. The proximal bowel was brought out as a colostomy.

The sigmoid segment was examined carefully and diverticula were noted but no malignant tissue.

Four days later a perineal resection of the rectal segment was done and the colostomy opened.

The rectal segment consisted of 13 cm. of terminal rectum. An ulcerated lesion was present 2 cm. from the proximal end. This ulcer measured 4.5 by 3 cm. and had raised, firm, rolled edges. Microscopic picture showed adenocarcinoma. The colostomy sloughed and retracted in the heavy fat layer of the abdominal wall. It required a secondary operation to bring the colon up to the surface and to excise the sinus tract. A transverse colostomy was accordingly established and the distal sinus allowed to close.

On Sept. 9, 1947, she was in good condition with a well-functioning colostomy and no signs of cancer. In March, 1950, she was in excellent health.

CASE 10 (257019).—A. B., a 66-year-old woman, was admitted to the Strong Memorial Hospital on Dec. 4, 1946.

In 1942 she had trouble with her bowels, with some blood in the stools. Barium enema studies showed diverticula. She got along very well on a smooth diet with only occasional blood in the stools following this.

In April, 1946, she had chills and fever with soreness in the left lower quadrant. She was sent into a hospital where she received penicillin and sulfadiazine. In two weeks her symptoms subsided. Roentgenograms again showed diverticulitis. On return home, fever recurred and sulfa drugs were started again. She was hospitalized in July, 1946, had a cyst of the ovary removed and a colostomy performed. Biopsy showed "inflammatory tissue" at that time. Bilateral phlebitis developed and she continued to take sulfa drugs until two weeks before admission to Strong Memorial Hospital. She had lost thirty-nine pounds since April, 1946.

Examination showed a poorly nourished, chronically ill woman. There was a colostomy in the midline below the umbilicus. Below this to the left was a firm, slightly tender mass which measured 8 by 8 cm. Liver was not palpable.

The red blood count was 2.8 million, hemoglobin 7.9 Gm., white blood count 10,200, polymorphonuclears 72, lymphocytes 28.

Barium enema was unsatisfactory. It showed a very irregular filling defect in the upper rectum. The sigmoid was poorly outlined and ragged in appearance. Proctoscopic examination revealed an inflammatory lesion but digital examination indicated a fungating mass suggestive of carcinoma. Biopsy showed only inflammatory tissue. Repeated proctoscopic examination ten days later showed an inflammatory mass with pus pouring from the lumen. Biopsy of this material showed inflammatory tissue only. At operation on Dec. 13, 1946, an abscess was entered on opening the peritoneum. The entire pelvis was occupied by a dilated rectosigmoid which was attached to the small bowel, tubes, uterus, and bladder on the left side.

The inflamed mass was separated from the hollow of the sacrum and the posterior wall of the uterus. The rectum was divided below the mass and closed over with inverting sutures. Drainage was provided through the perineum after removing the coccyx.

Gross specimen showed 30 cm. of resected rectosigmoid. The central mass consisted of densely bound loops of bowel filled with fungating necrotic tissue. Several diverticula were present. Microscopic examination revealed adenocarcinoma with acute and chronic inflammation.

Convalescence was stormy for a few days with distention and atelectasis. Improvement was steady following this. She was discharged eighteen days after operation on Jan. 19, 1947. She received 4,600 r in air over the lower abdomen.

She had gained weight and had a well-functioning colostomy one year after operation. On March 4, 1950, her physician reported that she was "doing very well indeed."

CASE 11 (286407).—E. C., a 74-year-old woman was admitted to the Strong Memorial Hospital on Sept. 28, 1948.

Six weeks previously she had noted gradual onset of a steady, severe, dull, aching pain in the left lower portion of her abdomen. The pain did not radiate. It remained constantly present until one week previously when it had lessened considerably. Since then she had had a very tender "bunch in this region."

Two days before admission she had a hard shaking chill with a fever recorded at 100.6° F. There had been no bloody or tarry stools and no pain on defecation. No diarrhea had been present but perhaps she had been more constipated than usual. Her appetite had been poor. She had lost twenty pounds in the last six weeks. She was known to be diabetic. One week before admission a barium enema showed diverticulitis with considerable spasm and poor filling of the rest of the colon.

Examination showed an alert, fairly well-preserved woman. The blood pressure was 180/100. There was an obvious mass in the left lower quadrant. It was acutely tender. There was a stricture in the anus which prevented rectal examination. The white blood count was 25,000. Wassermann reaction was 3+. The red blood count was 3.29 million, hemoglobin 9.7 Gm.

She was put on penicillin and under this medication the mass became smaller, the fever and leukocytosis subsided. She became ambulatory, without complaints, and the mass disappeared. The bowel resumed regular function and the stools were guaiac negative. She was discharged on Oct. 11, 1948. The impression was diverticulitis with perforation and abscess.

She was readmitted to the hospital on Nov. 2, 1948. She had felt well until one week previously when the steady, dull, abdominal pain returned in the paraumbilical area. She appeared chronically ill and pale. There was a rounded tender mass in the left lower quadrant, freely movable.

The red blood count was 4.4 million, hemoglobin 12.5, white blood count 15,000. Stool guaiac negative. Barium enema showed an irregular narrowed area corresponding

to the palpable mass. A few small diverticula were seen also in the same area and a fleck of barium which could represent a small ulceration. The possibility of carcinoma was suggested by this examination.

A big mass was found in the left lower quadrant at operation on Nov. 15, 1948. This mass consisted of matted omentum, small intestine, and sigmoid which were removed in one piece with wedges of mesentery. Two end-to-end anastomoses restored the continuity of the small and large intestines respectively. There was a hard nodule palpable on the under surface of the right lobe of the liver. It was thought to be a gallstone but because of adhesions could not be visualized. Much edema was found in the region of the mass. The lesion was believed to be carcinoma and diverticulitis combined. This was confirmed by pathology examination which showed adenocarcinoma of the sigmoid with extension to the mesentery and to the small bowel. There was also inflammation about the diverticula.

She had a prolonged convalescence but was discharged in good condition one month after operation. At follow-up examination on Jan. 20, 1949, a hard mass in the epigastrium was palpable. It was undoubtedly metastatic cancer in the liver. She was followed at home by her local physician who treated her symptoms as required. She died on Mar. 23, 1949.

CASE 12 (290461).—J. C., a 60-year-old man, was admitted to the Strong Memorial Hospital on Dec. 28, 1948.

For one and one-half years he had had intermittent left lower quadrant pain with blood and mucus in the stools.

Roentgenograms taken at an outside hospital showed "diverticulitis." Under treatment he had improved and had no trouble till seven months previously. Then he had a fever for three weeks and was hospitalized. Sulfa drugs and penicillin were given. He went back to work as a draftsman. One month before admission pains came again, crampy in nature, radiating to the left lower quadrant. He gave up work, his appetite failed and he lost thirty-five pounds in weight. He had to take laxatives to get bowel movements which were liquid in quality. There had been soreness of the bladder and nocturia once or twice.

He appeared to have lost weight and looked pasty. His blood pressure was 160/90. Liver was not paplable and there was no distention.

There was a sensitive palpable mass in the left lower quadrant. He showed external hemorrhoids.

He brought four series of x-ray films which showed diverticulitis with spasm in the sigmoid area in the first series, progressive narrowing of the segment in the intermeditae series, and almost complete obstruction in the last series.

Stool examination showed blood. The red blood count was 3.1 million, with hemoglobin 11.5 Gm. and white blood count 6,800. At operation on Jan. 5, 1949, there was a large mass of tissue in the left lower quadrant, matted together by adhesions to the bladder and to the small intestine. Considerable edema was present, also. A wedge of bladder and the loop of small intestine with its mesentery, were divided and removed still attached to the sigmoid segment. The bladder was repaired in two layers and end-to-end anastomoses were made between the small bowel and large bowel loops.

The gross specimen consisted of an extremely hard and irregular mass of tissue consisting of 20 cm. of small intestine, 15 cm. of sigmoid colon and bladder wall 7 cm. by 6 cm. There was dense, gritty, fibrous tissue and two fistulas between the large and small intestine. There were several hard white nodules in the mesentery measuring 2 mm. Microscopic examination showed carcinoma of the sigmoid with inflammation but no extension to the surrounding viscera. Convalescence was uneventful. One year later he had regained his normal weight. There was some irritation of the rectal segment with discharge of bloody mucus but no evidence of recurrence was found. X-ray examination showed a normal rugal pattern in the area of operation with a slight narrowing.

CASE 13 (158453).—G. S., a 73-year-old man with arteriosclerosis and a hypertensive cardiac condition, was admitted to the Rochester Municipal Hospital on Dec. 28, 1948. He was in failure on admission with generalized edema. He had mainly a left-sided decompensation and hypoproteinemia. He gave a history of increasing difficulty in his bowel

movements. Instead of his usual two bowel movements a day, for the past two months he had had only one movement every other day. This movement was frequently tarry in appearance and smaller in caliber. Laboratory examinations showed red blood count to be 2.5 million, hemoglobin 5.0, hematocrit 19 per cent. Stools were formed, with blood clots and 4+ guaiac reaction. The total protein was 3.9 Gm. with albumin-globulin ratio 2.7/1.2.

He gradually improved under medical treatment over the next week so that a barium enema study was made revealing diverticulosis of the sigmoid with no evidence of irritability or spasm. A second study of his gastrointestinal tract three weeks later revealed a normal cecum and numerous diverticula in the sigmoid with some evidence of a mild inflammatory reaction in this region. On sigmoidoscopic examination an area of ulceration was found and biopsy showed it to be adenocarcinoma. At operation on Feb. 18, 1949, a constricting annular lesion was found at the rectosigmoid junction. This area was excised and an end-to-end anastomosis was made. He made a slow recovery after operation but had no complications. He was discharged to a nursing home in good condition on March 20, 1949.

He was admitted to the Rochester Municipal Hospital on April 20, 1951, for ankle edema and exertional dyspnea which had become prominent in the past four months. His bowel function had been excellent. Barium enema showed diverticulosis of the sigmoid but was otherwise negative. He made a good recovery and was discharged to a nursing home on May 21, 1951.

CASE 14 (307319).—H. S., a 66-year-old man, was admitted to the Strong Memorial Hospital on Jan. 15, 1950.

For about one year he had noted blood on the toilet paper. About six months previously he had occasional lower abdominal cramps and excessive gas. Four months previous to admission he had blood-streaked stools. He was sigmoidoscoped and the only lesion noted was an anal fissure. He continued to pass bloody mucus although he was on a low roughage diet and Metamucil. On Jan. 4, 1950, a partial obstruction was noted in the mid-sigmoid on sigmoidoscopic examination. Barium enema showed a filling defect in the mid-sigmoid with many diverticula. There had been no weight loss.

Examination revealed a well-nourished, healthy-looking man. A sense of resistance could be made out in the left lower quadrant but no mass could be palpated.

The red blood count was 5 million, hemoglobin 14.22 Gm., white blood count 7,850. The stools appeared grossly bloody.

At operation the descending colon was studded with pea-sized diverticula. The mid-sigmoid had a hard mass of tissue and it was attached at this point to the mesentery of the small intestine. It separated without giving evidence of involvement of the mesentery. A wedge resection of the sigmoid and its mesentery was carried out. An end-to-end anastomosis was made.

Recovery was without incident. He was discharged on Feb. 1, 1950.

Pathology study showed 20 cm. of large bowel with adherent indurated mesentery. Diverticula were present and a large hard irregular ulcerative lesion. This measured 7 by 6.5 cm. Microscopic sections showed adenocarcinoma and hyperplastic lymph nodes.

CASE 15 (177666).—F. D., a 74-year-old man, was admitted to the Rochester Municipal Hospital on June 22, 1950. He had been constipated for many years and got relief by cathartics. In the six weeks previous to admission he noted mild anorexia, loss of eight pounds in weight and less response to the cathartics. During the last month his bowel movements had decreased markedly. His abdomen became distended. In the week previous to admission he had had only one small watery passage from the rectum. Five months previously he had noted a blood-streaked stool, but no bloody or tarry stools since then. For two weeks he had had generalized abdominal cramps. He vomited a few times during the week before admission.

He had had typhoid fever at ten years of age. In 1941 he had had an attack of jaundice of twelve days' duration. His mother and brother had died of tuberculosis.

He was well developed and well nourished. His abdomen was soft and there were no masses or tender points. Bowel sounds were present. On rectal examination a small

nodular movable mass was palpable high up. Blood was present on the examining glove finger. On laboratory studies, no anemia was found. Total blood proteins were 4.9 with albumin-globulin ratio 3/1.9. Sigmoidoscopic examination showed some small areas which were perhaps polypoid. Biopsies were taken which showed rectal polyps. Barium enema revealed multiple diverticula of the sigmoid and a complete shutoff in the region of the splenic flexure.

At operation a large mass was found in the descending colon about five inches below the splenic flexure. There was a firm nodule in the right lobe of the liver suggestive of metastasis. A resection of the descending colon with an end-to-end anastomosis was performed. Four days after operation he died. The diagnosis appeared to be pulmonary embolism or coronary occlusion. No post-mortem examination was made.

The pathologic specimen showed adenocarcinoma of the rectosigmoid with extension through the parietal wall and with an abscess cavity. There was a soft polypoid mass running through the lumen for a distance of 7 cm. Multiple diverticula were present with chronic inflammatory changes about them.

CASE 16 (308586).—I. W., a 71-year-old man, was admitted to the Rochester Municipal Hospital on Feb. 19, 1950, because of inability to void. His difficulty in voiding had increased over the past five years, consisting in frequency, difficulty in starting the stream, and terminal dribbling. He had had nocturia three to four times, and two days previous to admission had to be catheterized. He had not voided since then.

On examination he was well nourished. He had a distended bladder and an enlarged prostate. His blood pressure was 200/96. Laboratory studies showed nothing remarkable except inflammatory cells in the urine.

On further study it was found that no barium could be passed beyond the rectum. There seemed to be a block at the rectosigmoid junction.

He then remembered that for six or seven years he had had rectal bleeding with episodes of diarrhea of one to two days' duration. These alternated with periods of constipation. He had begun to take pills one year previously which gave watery movements.

At sigmoidosocpic examination a flat, discoid, mucosal lesion was noted at 12 cm. Biopsy was done and a diagnosis of carcinoma was made.

On Feb. 27, 1950, an abdominoperineal resection was carried out without incident. Following operation he had some minor difficulties in fluid balance which were straightened out by transfusion.

The pathologic specimen showed adenocarcinoma of the sigmoid. There were polyps showing malignant degeneration in the rectal segment below it and numerous diverticula in the segment above it.

On March 30, 1950, a retropubic prostatectomy was done for benign prostatic hypertrophy. He recovered from this second operation and was discharged in good condition with a well-functioning colostomy on April 15, 1950.

He was admitted to the Rochester Municipal Hospital again on May 14, 1951, for mid-epigastric pain. After careful study, an old pyloric ulcer with obstruction was diagnosed. A posterior gastrojejunostomy was done. A nodule in the right liver was removed and a diagnosis of bile duct adenoma made by microscopic examination. On June 8, 1951, an enteroenterostomy was done to relieve an obstruction at the previous posterior enterostomy site. A wound infection followed. This began to granulate and heal in by August, 1951. Otherwise his general condition remained stationary.

CASE 17 (43813).—G. W., a 71-year-old woman, was admitted to the Strong Memorial Hospital for the ninth time on Aug. 28, 1950. Her previous admissions had been for chronic constipation, nephroptosis, chronic cystitis, chronic sinusitis, herpes zoster, acute laryngitis, and acute otitis media. On this occasion she complained of rectal bleeding. She had noticed bleeding intermittently for three to four years—usually bright red followed by darker or black blood. It was never large in amount. She attributed it to "piles." There had been occasional cramps in her lower abdomen with the bleeding episodes. There had been chronic dysuria and frequency with these attacks.

There had been a more severe attack three weeks previously and she had consulted her physician who sent her to the hospital for study.

Examination revealed a well-developed, well-nourished woman. Her general condition was excellent except for a slight anemia (hemoglobin 11.7 Gm., red blood count normal). No abnormalities were detected on examination.

Barium enema studies showed a definite pathologic process involving the sigmoid. A few small diverticula were noted, and also a persistent defect in the proximal part of the sigmoid with an irregular margin. The loops could not be separated sufficiently to visualize this area, and very little barium could be passed proximal to it. The roentgenologists would not make a definite diagnosis of cancer.

A sigmoidoscope was passed 16 cm. without difficulty. An ulcerated, somewhat polypoid area was encountered above this. It bled easily but the tissue removed showed only acute inflammatory reaction.

At operation there were many adhesions between the small bowel and the anterior abdominal wall. A benign polyp was palpated in the sigmoid and farther down at the rectosigmoid junction there was a carcinoma as well as diverticulitis. A wedge resection including all those areas was done and an end-to-end anastomosis made low down in the rectum.

The pathologic sections showed a carcinoma of the sigmoid with one lymph node metastasis, a benign polyp of the sigmoid, and multiple diverticula with acute and chronic inflammation.

She was discharged on Sept. 22, 1950, in excellent condition. Her recovery from operation was without incident.

Her physician reported that she died in California during 1951—the exact date not specified. There was carcinoma present at the time of death.

CASE 18 (129062).—J. W., a 91-year-old man, was admitted to the Strong Memorial Hospital on Jan. 30, 1951.

He had had a history of chronic constipation going back for more than eleven years. Various cathartics had been taken for this. In August, 1950, he had begun to have blood and mucus in his stools. In December, 1950, he had had a barium enema study which showed diverticulitis of the sigmoid with partial obstruction. Since that study he had become more constipated than before. His last bowel movement had been thirty-six hours before admission. The night before admission he started vomiting and became distended.

For years he had had chronic cough and sinusitis. These conditions were treated by antibiotics and autogenous vaccines. He had become very deaf.

Examination revealed a well-preserved old gentleman. He had numerous senile keratoses. The abdomen was greatly distended especially in the lower quadrants. A right inguinal hernia was visible.

Laboratory studies showed the red blood count to be 3.8 million, hemoglobin 11.3 Gm., white blood count 10,300.

At operation there were greatly distended small bowel and large bowel loops, and free cloudy fluid. Exploration was difficult because of the distention. There was a perforation in the sigmoid at the rectosigmoid junction and a hard mass of tissue in the retroperitoneal area. It was thought that either a diverticulum had perforated into this area with formation of an abscess, or that a carcinoma had perforated and extended through the retroperitoneal tissues. A colostomy was made in the sigmoid loop.

Convalescence was complicated by persistent small bowel distention. This was finally relieved by passage of a Harris tube. The colostomy functioned well. He was taken home on Feb. 21, 1951. At home he began to discharge pus around the colostomy opening and through the rectum. This continued intermittently for several months. He ran a fever whenever the purulent discharge stopped. He gradually declined in strength and died on May 4, 1951.

Post-mortem studies revealed acute and chronic diverticulitis of the sigmoid colon and carcinoma with local pelvic extension and metastasis to the liver and lung (1 cm. lesion found). There were numerous other lesions of senile degeneration. The prostate contained several soft areas of primary carcinoma.

CASES THOUGHT TO BE CANCER, PROVED TO BE INFLAMMATION

CASE 1A (99697).—T. G., a man 60 years old, was admitted to the Strong Memorial Hospital on Mar. 7, 1935, with a history of three and one-half years constant dull pain in the umbilicus, occasionally lasting three to four weeks and cleared by Agarol. Four months previously he had had an attack of intermittent wandering pains relieved by enema. Two months previously he had had acute pain below the umbilicus which was constant, sharp and lasted one-half to one hour. His abdomen was sore and his temperature was 100° F. He also had chills. He was constipated, had ribbon stools, but there was no blood on the stools on examination.

He was a well-developed, plump, ruddy male who had general arteriosclerosis. Blood pressure was 190/85, hemoglobin 90 per cent, prostate enlargement 3+, stool guaiac negative. A walnut-sized, very tender, hard, submucous mass was found on rectal examination in the hollow of the sacrum.

Laboratory examination showed no ulceration, but redness was seen by proctoscopic examination. Barium enema showed a stricture at the rectosigmoid.

The patient was discharged to arrange for operation. Dysuria was present in the two weeks following this.

Operation was carried out on March 27, 1935, and what appeared to be a puckered napkin ring carcinoma with invasion of the bladder was found. Resection and an end-to-end anastomosis was done.

Microscopic examination showed acute and chronic inflammation in the sigmoid which was narrowed and full of diverticula. No carcinoma was present.

CASE 2A (139418).—L. S., a 50-year-old woman was admitted to the Strong Memorial Hospital on April 13, 1938. She was well till two weeks before admission. Then she began to have difficulty in moving her bowels. This became gradually worse and for the ten days before admission she had had movements only with cathartics or enemas. There was cramp-like low abdominal pain, not radiating, and vomiting on two occasions. During the past year, several times, she had noted bright blood on the toilet paper. There had been no weight loss, chills, or fever.

She was obese and did not appear acutely ill; temperature was 37° C., pulse 78. The abdomen was distended, tympanitic, and dull in the flanks; no fluid wave could be made out. Nothing else of importance was noted.

There was no anemia but the white blood count was 12,400 on blood study. The stool guaiac was negative.

Diagnosis of incomplete low intestinal obstruction was made and confirmed by barium enema which showed complete obstruction at the rectosigmoid. Cecostomy was done under local anesthesia. The patient developed cystitis and was placed on tidal irrigation. Cystoscopy showed edema of the trigone with some polyps near the vesical orifice. She developed a mass in the pelvis and continued to run a septic course. The diagnosis was made of perforation of either diverticulum or of carcinoma with abscess formation. At operation a colon abscess was drained, due to perforation of a diverticulum. She did not do well following this procedure and died on June 15, 1938. No evidence of carcinoma was found at operation but a pathology examination was refused.

CASE 3A (139355).—H. C., a 62-year-old man, was admitted to the Strong Memorial Hospital on April 15, 1938.

He had been in failing health for a year. There was decrease in strength, loss of fifteen to twenty pounds and a little tendency toward constipation. Five days previously he had had nausea and vomiting with vague aching in the right paraumbilical region. Marked obstipation developed in spite of frequent enemas. Vomiting of a severe type and fecal in character was present according to his local physician. There had been no melena or bloody stools.

He was emaciated, acutely and chronically ill. The general examination showed nothing significant. The blood pressure was 135/40. There was moderate peripheral arteriosclerosis.

There was no anemia. An electrocardiogram showed coronary disease with myocardial damage. Barium enema revealed an almost complete obstruction at the rectosigmoid junction. It was regarded as almost certainly carcinoma. The large bowel was distended above the obstructed zone.

On April 19, 1943, a cecostomy was performed under local anesthesia.

At operation on April 23, 1938, many loops of small bowel were adherent to the sigmoid in the pelvis. These were carefully freed. A low grade inflammatory reaction was present. The epiploa were porky. A stout band of adhesions ran across the middle third of the sigmoid. This band was released. No evidence of carcinoma was found.

He was discharged on May 9, 1938 in good condition and without complaints.

In December, 1938, he had a transient cerebral vascular accident with a ptosis of the right eyelid and a divergent squint. He was in good condition as far as his large bowel was concerned. Since that date it has been impossible to locate him.

CASE 4A (166571).—W. B., a 65-year-old man, was admitted to the Rochester Municipal Hospital on June 22, 1940. Three days before admission he was awakened by a sharp, crampy abdominal pain. There were thirty to forty bowel movements consisting of blood and mucus. There had been no previous constipation, diarrhea, or tarry stools, and no weight loss.

He did not appear ill. His temperature was 38.5° C., pulse 92, blood pressure 180/100. His heart was enlarged and there was a systolic murmur at the apex. There was considerable tenderness in the middle of the lower abdomen, more on the left than on the right.

There was no anemia. The white blood count was 12,200. The stool was guaiac positive. An electrocardiogram showed auricular fibrillation. Barium enema showed an almost complete obstruction at the midsigmoid but no gaseous dilatation of the bowel above it.

He was explored on June 24, 1940. A large indurated mass was found in the region of the sigmoid at the brim of the pelvis. There was considerable inflammatory reaction of the tissues in this region. No evidence of metastases could be found. A cecostomy was done.

At operation on July 11, 1940, several loops of small intestine were found to be adherent to the sigmoid. These were dissected free and a small abscess cavity was uncovered. The sigmoid was delivered by freeing it from the lateral wall to which it was adherent. It contained a stony hard mass 6 to 8 cm. in diameter. The sigmoid was resected and an end-to-end anastomosis made.

Postoperative course was uneventful. He was discharged in good condition, much improved.

Pathology examination showed a tough fibrous tumor. It was acute and chronic inflammation only, with no evidence of malignancy on microscopic study.

In December, 1941, he was admitted to the County Hospital with decompensated hypertensive and arteriosclerotic heart disease. He improved under rest and digitalis and was discharged later in the month.

CASE 5A (168733).—E. G., a 48-year-old woman, was admitted to the Strong Memorial Hospital on Dec. 7, 1941. For one month she had noted pain, tenderness, and a hard lump in the left side of the abdomen. She began to have constipation and small movements, never bloody or tarry. Catharties gave no relief.

Her temperature was 37.8° C., pulse 80. She did not appear ill. In the left lower quadrant there was an orange-sized mass which was fixed and nontender. Pelvic examination showed that the uterus was displaced toward the right.

There was no anemia. The white blood count was 10,300.

The gynecologists made a diagnosis of ovarian tumor as this woman had had a myoma previously treated with radium. No barium enema studies were done. At operation, they were surprised to find that the tumor involved the descending colon and sigmoid. Diagnosis was next considered to be carcinoma. The surgeons consequently excised the tumor and did an end-to-end anastomosis.

The gross specimen showed an irregular, gray, necrotic, firm, constricting lesion with numerous deep, ulcerated crypts and pockets. Microscopic examination showed acute and chronic inflammation.

When last seen in April, 1942, she was in excellent condition.

CASE 6A (199682).—T. H., a 46-year-old man, was admitted to the Strong Memorial Hospital on Jan. 5, 1943.

He had had a diagnosis of ruptured gastric ulcer three years previously but had refused operation. After two or three weeks he recovered. Since that time he had had constipation and abdominal pain, varying in intensity. About three months before admission he had had another attack of pain which had continued to the present. He had lost his appetite and also thirty pounds in weight.

His temperature was 36.5° C., pulse 88. He was poorly nourished with evidence of recent weight loss. There was a tender mass 6 by 8 cm. in diameter in the epigastrium.

There was no anemia. The white blood count was 15,600. Stools were guaiac negative.

Barium enema showed a persistent filling defect to the left of the midline in the transverse colon. It appeared to be at the upper border of a large tender mass which occupied the space below the transverse colon and medial to the descending colon. No diverticula were seen. The small bowel showed a dilated loop in the region of the mass. The radiologist interpreted these films as possible carcinoma of the transverse colon with perforation, abscess, and secondary partial small bowel obstruction. However, the appearance in the transverse colon might have been spasm secondary to a primary lesion in the small intestine.

Operation on Jan. 12, 1943, showed an abscess cavity completely walled off by an inflammatory mass. It was impossible to tell whether it was consequent to a perforated cancer or to a perforated diverticulum. It was drained.

The subsequent course showed that the diagnosis was not carcinoma. The patient was followed for three years without any evidence of it.

CASE 7A (260250).—H. R., a 54-year-old woman, was admitted to the Strong Memorial Hospital on Feb. 23, 1947. She had had intermittent constipation for the past year. In August, 1946, she first noticed bloody streaking on the toilet paper. Over the last five months the constipation had increased, the stools had diminished in caliber, and there had been tenesmus. She had lost her appetite, become weak, and lost fifteen pounds in weight. There were bouts of low abdominal pain, not severe, and frequent passage of small amounts of mucus and blood. She had been treated for anemia and hemorrhoids by her physician until three weeks before admission. At that time a proctoscopy revealed a growth in the rectum.

She had had a hysterectomy for fibroid tumor at the Mayo Clinic in 1927. The right ovary and appendix were removed at this operation.

She appeared pale, anxious, and chronically ill. There was a midline abdominal scar. The rectal examination showed a narrowing at 6 to 7 cm. with a mass which was firm, fixed, and not tender. The impression was that there was an almost complete obstruction and a "frozen pelvis."

The red blood count was 4.2 million, hemoglobin 12.1, and white blood count 11,800.

Barium enema showed an obstruction in the rectum, and the patient could not retain barium because of irritability of the bowel. No evidence of spread was made out on a metastatic survey. Proctoscopic examination showed an obstruction at 3 inches from the anus. A bit of hard tissue was removed by passing the forceps through the narrowed opening. It suggested carcinoma but microscopic examination failed to reveal malignancy, showing only chronic inflammation.

The scar of the previous operation was excised on Feb. 26, 1947. Many adhesions were present. There were no metastases in the liver. The pelvis was densely matted with scar and the terminal ileum was bound down in the pelvis with a sharp kink, partially obstructing it. A lateral anastomosis was made between the terminal ileum and the cecum. A hard node in the mesentery was removed for biopsy. A transverse colostomy was done dividing and separating the loops. It was considered a palliative operation for advanced carcinoma.

The lymph node revealed only hyperplasia on microscopic examination. Nevertheless it was decided to treat her with radiation therapy in the hope that the condition might be made operable. Accordingly this was done until she had received a total of 2,880 r, midpelvic dose.

Another proctoscopy was done on March 23, 1947, but still no malignant tissue could be obtained.

Her general condition remained so good that the diagnosis of carcinoma was questioned. Repeat barium enema studies of the sigmoid segment were made from the distal colostomy and by rectum on Dec. 3, 1947. The barium from below went to the rectosigmoid junction; that from above showed marked spasticity of the sigmoid, irritability, and several diverticula. The diagnosis was changed to diverticulitis with old perforation and partial obstruction.

Repeated proctoscopic examination under anesthesia on March 31, 1948, showed that the rectum was quite fixed with scar tissue so that it would not be moved. It was possible to pass the scope for 6 inches, but not beyond this point. The area near the obstruction was edematous.

On July 19, 1949, she had gained ten pounds in weight. She looked well and her colostomy functioned well. She did not want any further operations as she was satisfied with her status. Barium enema on July 27, 1949, was not essentially different from that of March 31, 1948.

She remained in good health until last seen in February, 1952.

CASE 8A (209).—B. S., a 60-year-old man, was admitted to Strong Memorial Hospital on Dec. 18, 1949.

For fourteen years he has had diverticulitis of the sigmoid with bouts of pain, fever, and leukocytosis. Barium enema in 1939 showed a local area in the sigmoid three inches in length with diverticula and spasm. He had several attacks which required bed rest and sedation. In one attack there was moderate bladder irritation. In 1942, he had a severe attack. A barium enema was done a few months later and barium was seen to escape into the peritoneal cavity. An abscess developed but drained spontaneously by rectum. Since 1943 there had been transient attacks of abdominal pain. Barium enema Dec. 4, 1949, showed considerable scarring and possible spasm. There had been no weight loss. He had had two types of bleeding from the rectum—bright red blood in small amounts, and occasionally dark, blood-stained mucus. The caliber of the stool was unchanged.

His physician noted a polyp high in the rectum on proctoscopic examination. General examination showed him to be in good physical shape. There was blood in the stool on several examinations. The red blood count 6 million and the hemoglobin 19.1 Gm. Because of the blood in the stools and the scarring of the sigmoid area by x-ray, his medical attendants and the radiologist were unwilling to accept the responsibility of watching the progress. Accordingly, he was explored on Dec. 20, 1949. The sigmoid was densely adherent to the lateral wall and to the bladder. These adhesions were divided by sharp dissection separating the bladder from the sigmoid without entering either organ. The lesion in the sigmoid felt stony hard. A segment of sigmoid and mesentery were resected. An end-to-end anastomosis was done. It was impossible to be sure whether the sigmoid lesion was inflammatory or neoplastic until it had been examined microscopically. The gross specimen showed 19 cm. of sigmoid colon with attached mesentery. The wall of the sigmoid was indurated and thickened and edematous. Many diverticula were present. Microscopic sections showed chronic inflammation with focal lymphoid infiltration.

Convalescence was without incident. He was discharged on Jan. 2, 1950. He returned to light work as a farmer within three weeks following his operation and has remained well until February, 1952.

CASE 9A (63406).—C. B., a 64-year-old man, was admitted to the Strong Memorial Hospital on Nov. 15, 1950. He complained of frequent bloody bowel movements.

Ten years previously he had been admitted to this hospital with diarrhea, chills and fever, and left lower abdominal pain of five weeks' duration. Barium enema revealed diverticulitis of the sigmoid. His symptoms disappeared and he was discharged after two weeks in

the hospital. Since that time he had had no recurrence of these severe complaints until four and one-half months previously. He had had occasional slight fever and constipation but his physician kept him in bed and gave him "sulfa" drugs which gave him relief. Four and one-half months previously he had experienced lower left quadrant cramps accompanied by frequent movements. Blood was noted either at the beginning or at the end of the movement. Frequent bloody stools continued up till one month previously and constipation became more pronounced. He lost twenty pounds during this period. During the acute episodes he had marked leukocytosis and always pyuria. For several months there had been a bulging in the left lower abdomen and a mass was felt there by his physician.

In his past history he had had benign prostatic hypertrophy and prostatic calculi relieved by transurethral prostatectomy in July, 1945. A peritonsillar abscess was incised and drained in February, 1947.

Examination showed a well-developed man in no distress. He showed evidence of recent weight loss. The heart was slightly enlarged and there was a blowing murmur in the aortic area. The blood pressure was 165/85. There was some sclerosis of his peripheral vessels. The lower abdomen was distended and there was a tender mass, sausage shaped, about 10 cm. in length, very slightly movable, in the region of the sigmoid. Rectal examination was not contributory.

Laboratory studies showed a few white blood cells and red blood cells in the urine. There was evidence of a moderate anemia.

He was given transfusions to restore his blood loss and even though he ran a fever daily it was decided to operate on him as he showed increasing signs of obstruction. He was given Aureomycin and penicillin for two days, after which a resection was made of the soggy, inflamed, involved sigmoid. An immediate end-to-end anastomosis was done. Convalescence was without incident. His bowel functioned nicely within a day of operation. He was discharged in excellent condition eleven days after operation.

Pathology studies showed acute and chronic diverticulitis with ulceration and granulomatous reaction.

He has had no return of symptoms or intestinal trouble to the present.

CASE 10A (311643).—W. B., a 71-year-old, retired businessman, was admitted to the Strong Memorial Hospital on May 3, 1950.

He had been well until about six weeks previously when he developed a persistent diarrhea, productive of eight to ten stools per day. The stools were unformed and brown without evidence of gross blood or mucus. Later they became black perhaps due to some medication given by his physician. There were intermittent mild gas pains associated with the diarrhea. The pains were in the lower abdominal area, relieved by change in position. Chloromycetin was used for ten days ineffectually but dilute HCl three times a day apparently helped. His bowels moved only four to five times a day and the stools were formed. This corresponded to his usual bowel habits of the past ten years. During the acute diarrheal attack he lost fourteen pounds but during the week before admission he regained eight pounds.

He was a well-developed, well-preserved man in no apparent discomfort. Aside from slight tenderness in the left lower quadrant there were no abnormalities in the physical examination.

There was a white blood count of 13,800. The stool examination showed mucus, white blood cells, and red blood cells. Culture was negative for enteric pathogens. Repeated stool examinations showed blood on one occasion and no blood on another study.

A barium enema revealed a persistent narrowing of the sigmoid, numerous diverticula, spasm, and irritability. Sigmoidoscopic examination showed an obstructing lesion in the sigmoid, the nature of which could not be determined.

After preparation on aureomycin and low residue diet operation was done. There was a hard mass of tissue in the region of the rectosigmoid densely adherent to the surrounding structures. Adherent omentum was divided, but the bladder fortunately was dissected off without entering it. The point of greatest fixation was in the hollow of the sacrum just

beyond the brim of the pelvis. Diverticula were present way down into this rectal segment. The whole mass of tissue was removed en bloc with a wedge of mesentery. An end-to-end anastomosis was made low in the pelvis.

He did well following operation except for the bladder which became obstructed. Study showed a benign prostatic hypertrophy. A retropubic prostatectomy was done without incident.

He left the hospital in good condition on June 16, 1950.

Pathology studies showed diverticulitis of the rectosigmoid colon with the formation of a large extralumenal sinus cavity and a small abscess pocket. There were three polyps in the removed segment. The lymph nodes were hyperplastic. The prostate showed benign hypertrophy.

He was readmitted to the hospital on Dec. 26, 1950, because of an abscess in the abdominal wall scar. This was drained and compressed. He was discharged on Jan. 2, 1951, in good condition.

SUMMARY

1. Bleeding in presumed diverticulitis calls for a most careful evaluation.

2. In case a differential diagnosis cannot be made clinically between diverticultitis with complications and sigmoid cancer with complications, exploratory surgery is indicated.

3. Operation under such circumstances should be as radical as for carcinoma, taking all matted tissues out in one block.

4. The only certain way to differentiate complicated diverticulitis and sigmoid carcinoma with complications is by microscopic section.

5. It may be difficult to secure the proper tissue for accurate diagnosis because of the widespread inflammatory reaction around the process.

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GASTRIC RESECTION AS THE TREATMENT OF PERFORATED GASTRODUODENAL ULCER

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ALTHOUGH a long time has elapsed since Von Haberer, in 1919, first recommended gastrectomy for the treatment of perforated peptic ulcers, and although, in the meantime, many statistics have been published showing satisfactory results of this method, radical differences of opinion still exist among authors. Most of the surgeons of Continental Europe and Russia, following the example of Haberer, Finsterer, Judine, Duval and others, and being satisfied with the results obtained, consider gastrectomy the preferable method of treatment (with certain limitations) of perforated peptic ulcer, while surgeons of North America and England continue to favor minor procedures such as suture or, even more recently, continuous aspiration (Taylor). There is no doubt that the problem is not as simple as it looks from a first glance at statistics. A great number of factors are involved and must be carefully considered in order to draw correct conclusions.

The supporters of conservative methods of treatment rightly point out that the purpose of the operation is to save the life of the patient and not to cure a disease of long standing such as a peptic ulcer. They also believe that a great number of patients are being permanently cured by suture and that the performance of an amputating operation such as gastrectomy on young individuals with acute ulcers for whom prognosis is rather good, is not without unpleasant aftereffects.

The point of view of supporters of immediate gastrectomy in the treatment of perforation may be summarized in a few words as follows:

By this operation the patient gets rid of the ulcer and its attendant complaints. The hospitalization period is shortened and a second operation avoided. The operation is technically easy and the closure of the duodenal stump sure, since the ulcer usually occurs on the anterior surface of the stomach or the duodenum and near the pylorus, while a second operation is more difficult owing to the formations of adhesions, especially on a drained wound.

When we started performing gastrectomies for perforated ulcers in the Evangelismos Hospital, Athens, Greece, from 1932 to 1936 we had eighteen cases of perforation, which one of us (G. C.), in collaboration with Christeas, reported to the Academie de Chirurgie de Paris. Of those eighteen patients, gastrectomy was performed on thirteen without fatality, while the other five were treated by simple suture, with one death. Gastrectomy was performed within the first six hours after perforation on patients in good general condition.

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The sponsor of our work, Pierre Brocq, made a thorough study of the bibliography on the subject and defined the indications for gastrectomy, basing them upon the experience gained and relative statistics. Later, in 1949, Mialaret, in his monograph on the perforation of the Peptic ulcer, recognized our work as an inducement to perform such operations more frequently in France.

We now wish to present the cases of perforation which were admitted to the First Surgical Clinic of the University of Athens in the Laikon Hospital from Jan. 1, 1942, when one of us (G. C.) was appointed director of the clinic, to Jan. 1, 1951. During this time ninety-eight patients with perforated peptic ulcer were admitted to the clinic for treatment. Fifty-six were operated upon by gastrectomy with two deaths, a mortality rate of 3.57 per cent, thirty-nine had simple closure of the perforation with eleven deaths, a mortality rate of 28.2 per cent, and three had continuous aspiration (according to Taylor) without fatality. If to the above figures we add the previously mentioned thirteen cases of gastrectomy, then the total mortality rate is reduced to 2.9 per cent.

In the sex and age of the patients and in the position of the ulcer, there was no divergence from the typical findings. Of the ninety-eight patients, ninety-six were men and two women. Perforated peptic ulcer occurs with greatest frequency between 30 and 45 years of age. Two of our patients were 19 years old, one 72 years old. Location of the perforation is usually on the anterior surface of the stomach or duodenum and near the pylorus. Seven perforations were observed on the lesser curvature of the stomach and it is worth noting that five of these were seen in 1942, when the total number for this year was fourteen. The same predilection for the lesser curvature was noticed in all the other clinics in Greece at this period when the country, owing to the enemy occupation, was under difficult conditions of nutrition, and most of the population, especially the poor classes from which our patients have been drawn, was in a state of undernutrition and hypoproteinemia. One perforation was noted on the greater curvature exactly on the line separating the body from the fundus. Most of the operations were performed under local anesthesia with premedication by intravenous scopolamine and morphine, and a small quantity of ether was given by the open method until the closure of the duodenal stump. During the last two years we used a modern apparatus for anesthesia and we started utilizing from the very beginning a combination of Pentothal Sodium and ether-oxygen, limiting the use of local anesthesia even for gastrectomies performed *a la froid*. The operations are usually performed by the attending surgeons and a few of them by the residents under the supervision of attending surgeons experienced in gastrectomies, a great number of gastrectomies being performed annually in the clinic. As statistics reported by various authors reveal, the kind of operation performed is a significant factor in the prognosis. For this reason we limit the indication for gastrectomy to certain cases, reserving for the others more conservative operations. We side with the opinion that gastrectomy is

a more logical operation than others because its aim is curative rather than palliative. We also think the old notion that a large number of patients (more than 50 per cent according to De Bakey) permanently get rid of the trouble by simple suture, is incorrect. We are not guided by personal opinion alone. Recent communications in a careful postoperative follow-up of a large number of cases show that only 13.3 per cent of the patients treated by simple suture have remained free of symptoms, while the others have been under continuous medical and dietetic supervision and many have been obliged later to have a more radical operation. We believe that (gastrectomy when performed under suitable conditions and indispensable technical exigencies) has a mortality rate, as represented in our statistics, no greater than that of simple suture. Statistics and our experience show that the radical operation may be performed systematically on young and otherwise healthy individuals by surgeons experienced in gastrectomy without greater operative mortality than that of the more conservative operations. Our contention is strengthened by conditions existing in the period our statistics cover. During most of these years, we lacked means of resuscitation (blood plasma) and antibiotics. The malnutrition of our patients and the old type anesthesia were also serious handicaps. Only the gastrectomies of the last two years were performed with the help of contemporary means of resuscitation and ample supply of indispensable antibiotic medicines.

The criteria we employ to decide upon the performance of gastrectomies are given in the following paragraphs.

The time factor is taken into serious consideration. In our city there is a system whereby each hospital is on duty for twenty-four hours every week, where emergency cases, transported from first aid stations, are admitted immediately without objection or delay. In that hospital, residents under the supervision of an attending surgeon remain continuously on duty. Thanks to this system, it is possible for most patients to be admitted within the first hours after the perforation, before the symptoms of peritonitis have set in. We usually perform gastrectomies on patients admitted within the first eight hours after the perforation. It is not unusual to decide upon gastrectomy on patients whose perforation exceeds eight hours, as long as local findings during the operation appear satisfactory. Perforation on an empty stomach with a small quantity of liquids confined under the liver region without false membrane and with dilation of the first loops of the jejunum is not a contraindication for the operation. Based on experience to date, it is considered right to believe that the abdominal exudation remains sterile up to six hours after perforation or at least only slightly toxic.

The general condition of the patient is a factor of great importance. Apparent cardiopulmonary disorders, liver ailments or kidney lesions, a reduction of hemoglobin, or hypoproteinemia we consider contraindications.

The age of the person is another factor for consideration. Since the mortality rate is greater in individuals over 55 for any kind of perforation operation,

it is clear that for persons of advanced age gastrectomy should be avoided. As proof of a mistaken indication is the death which occurred in one of our cases.

A 72-year-old patient was admitted four hours after the perforation of a juxtapyloric ulcer. The general condition of the patient was satisfactory, there was no apparent cardiopulmonary disorder revealed by auscultation. The resident on duty, induced by the technical ease of the operation in this particular case and taking advantage of the temporary absence of the attending surgeon, proceeded with gastrectomy which resulted in the death of the patient from circulatory insufficiency on the fourth postoperative day.

Sometimes although rarely, for technical reasons, we are obliged to perform gastrectomy—as, for example, in the presence of a big callous ulcer with hard lips which would not permit closure by suture.

The presence of multiple ulcers, the possible narrowing of the duodenal lumen by the suture, and the localization of the ulcer on the stomach, also require gastrectomy because of possible degeneration. If we are obliged to avoid gastrectomy we can perform Balfour's or Neumann's epiploplasty.

We usually resect a large portion of the stomach (at least three-quarters) and we endeavor to obtain a good closure of the duodenal stump. We use a transmesocolic anastomosis with a short loop of Hofmeister-Finsterer type in three layers, having ligated previously the sub-serous vessels of the stomach. We almost always omit drainage, thinking it useless. Postoperatively we use aspiration with a Levin tube when needed.

Three cases were treated by the Taylor method (continuous aspiration) without fatality. The cases treated by aspiration were admitted twelve hours or more after the onset of the perforation and the peritoneal reaction was confined to the epigastrium and right hypochondrium.

SUMMARY AND CONCLUSIONS

Ninety-eight cases of perforated gastroduodenal ulcer are presented. In fifty-six gastrectomies there were two fatalities, a mortality rate of 3.57 per cent. Adding to these cases thirteen previously reported by us without fatality, we have sixty-nine cases with two deaths, a mortality rate of 2.9 per cent.

Thirty-nine patients were treated by simple closure of the perforation with eleven deaths, a mortality rate of 28.2 per cent, and three by continuous aspiration without fatality.

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THE EFFECT OF RUBBER TUBING ON THE HEALING OF COMMON DUCT ANASTOMOSES

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STRICTURE of the common bile duct has received considerable attention in the clinical literature. Most authorities agree that, when possible, end-to-end anastomosis of the proximal and distal segments of the duct is the procedure of choice. When doing end-to-end anastomosis it is generally agreed that a splinting tube inside the duct should be used.[1-7] Reference has been made in the literature by several authors[8-13] to the irritative action of rubber tubing on the biliary system, but no experimental work has been found regarding the effects of drainage with a rubber T tube on the healing of a common duct anastomosis.

In most dogs the common bile duct is of fine caliber and its wall is very thin. Other experimenters have ligated the common duct in a preliminary operation to secure a dilated duct large enough on which to work with ease.[11, 14-16] McWhorter[10] found that bile ducts became patent after ligation with catgut, and Hilsabeck and Hill[17] found that a nonabsorable suture could be removed from around the common duct after several days without a stricture developing at that site. Shapiro and Robillard[18] and Douglass and Cutter,[19] from their studies of the blood supply of the common duct, recommend freeing only the duct ends from the surrounding structures when performing end-to-end anastomosis. The present experimental problem was designed with proper attention to these findings.

Forty-eight male and female mongrel dogs, varying in weight from 15 to 36.5 pounds, were used. All animals were anesthetized, and aseptic operative techniques employed. Two operations were performed on all except four animals, which died before, or were sacrificed at the time of, the second operation. The first operation was performed through a right subcostal incision, and the common duct was ligated with a single silk thread tied close to the duodenum. Seven days later the abdomen was entered through the midline, and the previously applied ligature was removed by careful dissection. The extremely dilated biliary system was then decompressed through a large bore needle inserted in the dome of the gall bladder. The hole made by this puncture was closed by suture. The common duct was freed for a distance of approximately one centimeter and transected. In most instances this was done below the entrance of the bile duct from the right lower lobe. The anastomosis was accomplished in forty-four animals with interrupted 0000 chromic catgut on an atraumatic needle.

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In twenty animals a No. 10 French latex rubber T tube was inserted in the common duct above the anastomosis. A long arm of the tube was allowed to extend through the site of anastomosis, but not through the site where the constricting ligature had been removed. The tubes were fastened to the fascia and skin and allowed to drain to the outside. Three to five millimeters of the tubes were allowed to protrude from the skin margin, and the remainder was cut off. In twenty-four animals the same procedure was followed except that no T tube was used in the common duct. In one-half of these animals the abdomen was closed without drainage of any kind. In the other one-half the area adjacent to the operative site was drained with a No. 10 French latex rubber tube. However, we were unable to keep these drainage tubes in place longer than three weeks because the animals pulled them out in spite of average precautions.

Animals which survived both operations were sacrificed at sixty-one to sixty-four days after the second operation, except for two animals which were sacrificed at fifty-seven days. At autopsy, 1 to 2 c.c. of bile were aseptically aspirated from the gall bladder for culture. The liver, porta hepatis, first portion of the duodenum, and pylorus were then excised in block. The biliary systems were dissected free while the specimen was fresh. Note was made as to the amount of adhesions, presence or absence of drainage tubes, and presence of strictures and dilation by gross inspection. Following removal of the biliary ducts from the rest of the specimen, casts were made of the common duct in a number of cases using low-melting-point paraffin. Specimens of the common duct and the liver were fixed in 10 per cent formalin and stained by the hematoxylin-eosin method. Representative sections for microscopic examination were made above, below, and through the site of anastomosis of the common duct. Sections were also made of the liver.

TABLE I. OUTCOME OF 46 DOGS ON WHICH LIGATION AND SUBSEQUENT TRANSECTION AND ANASTOMOSIS OF THE COMMON BILE DUCT WAS PERFORMED

	ANASTOMOSIS WITH T TUBE	ANASTOMOSIS WITHOUT T TUBE OR DRAIN	ANASTOMOSIS WITHOUT T TUBE WITH DRAIN
Number of animals in each group	20	12	12
Number that lived and were sacrificed	12	5	11
Number of animals that died	8	7	1
Causes of death:			
1. Bile peritonitis	2	5	0
2. Liver abscess	1	0	0
3. Ruptured uterus	1	0	0
4. Evisceration	0	2	0
5. Bowel obstruction	2	0	0
6. Causes undetermined	1	0	1
7. Sponge abscess	1	0	0

During the two months of postoperative observation, none of the animals died from biliary obstruction. In two animals the T tubes could not be found at the time of sacrifice. Twenty-eight of forty-four lived until sacrificed, and sixteen animals died following the second operation. Causes of death according

to the various groups of animals are found in Table I. It will be seen that there was a mortality rate of 37 per cent in the entire group of forty-four animals, and a discussion of the causes of death seems warranted. It is not surprising that the principal cause of death was bile peritonitis. Almost one-half of the deaths were due to this condition. In the remainder, death in most instances is considered to be irrelevant to this study. It will be noted that bile peritonitis occurred primarily in the group of animals in which no method of drainage was employed. It may therefore be concluded that in repair of a transected common bile duct some form of drainage should be provided. McArthur[20] and others have clinically used a buried rubber catheter for end-to-end anastomosis, but have provided some method of external drainage.

TABLE II. RELATIONSHIP OF STRICTURE FORMATION TO TYPE OF OPERATION PERFORMED

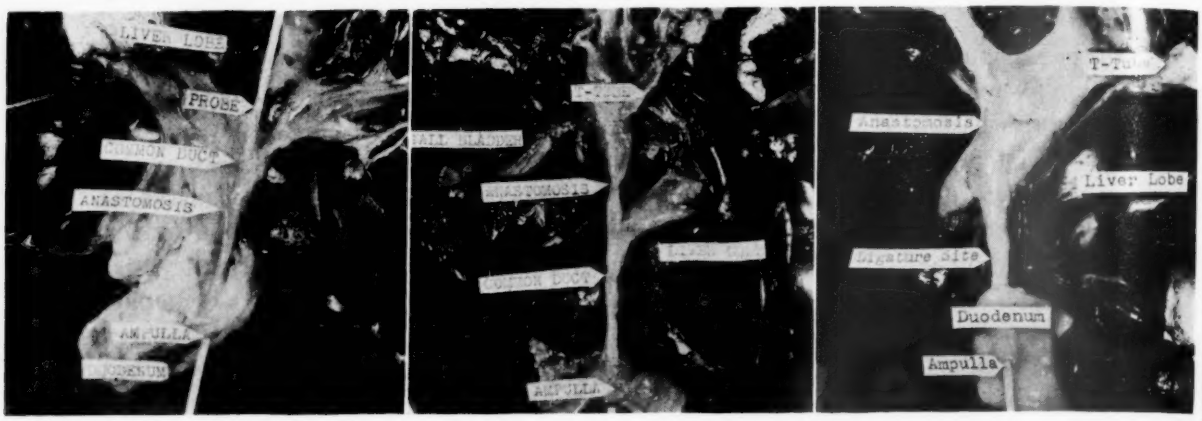
	ANASTOMOSIS WITH T TUBE	ANASTOMOSIS WITHOUT T TUBE OR DRAIN	ANASTOMOSIS WITHOUT T TUBE WITH DRAIN
Number of animals	12	5	11
Number of strictures	11	1	2
Strictures found at anastomosis	1	1	0
Strictures found at ligature site	10	0	2

Animals in which T tubes were placed had more dense adhesions than those where no T tube was used. The duodenum was frequently adherent to the undersurface of the liver, and at times, the gall bladder was adherent to the common duct or the duodenum. In animals with T tubes the entire common duct was thickened, dilated, and without its normal translucency. Eleven of 12 animals with T tubes had stricture formation, while stricture was present in only three of sixteen animals without T tubes. Narrowing of the duct was commonly present at both the site of ligation and the site of anastomosis, but dilation above the site of ligation made stricture formation less evident at the site of anastomosis. In one animal in which the long arm of the T tube did not extend through the site of anastomosis, stricture formation was most evident at that site. Fig. 1 depicts gross autopsy findings. Representative casts made of the common ducts may be found in Fig. 2. Table II shows the relationship

TABLE III. BACTERIA FOUND AT TIME OF SACRIFICE

	ANASTOMOSIS WITH T TUBE	ANASTOMOSIS WITHOUT T TUBE OR DRAIN	ANASTOMOSIS WITHOUT T TUBE WITH DRAIN
Number of animals	12	5	11
Positive cultures	12	3	6
Negative cultures	0	1	5
Number of cultures obtained	0	1	0
Bacteria found:			
1. *Escherichia coli**	8	1	0
2. *Shigella sonnei*	1	0	0
3. *Micrococcus saccatus*	1	2	5
4. *Neisseria Veillonella parvula*	1	0	0
5. *Aerobacter aerogenes*	1	0	0
6. *Escherichia freundii*	0	0	1

*Positive cultures of both *Escherichia coli* and another organism were found in two animals. These organisms were *Clostridium welchii* and *Streptococcus faecalis*.



A. *B.* *C.*

Fig. 1.—*A*, Specimen of a common bile duct which has been dilated, transected, and anastomosed in which no T tube was placed. The duct is translucent and no evidence of stricture is present. The hepatoduodenal ligament is seen posterior to the duct.

B, Specimen of a common bile duct which has been dilated, transected, and anastomosed over a T tube. The duct is thickened and stricture is evident at the site of anastomosis.

C, Specimen with T tube like *B* which shows thickening, dilation, and maximal stricture formation at the site of previous ligation.

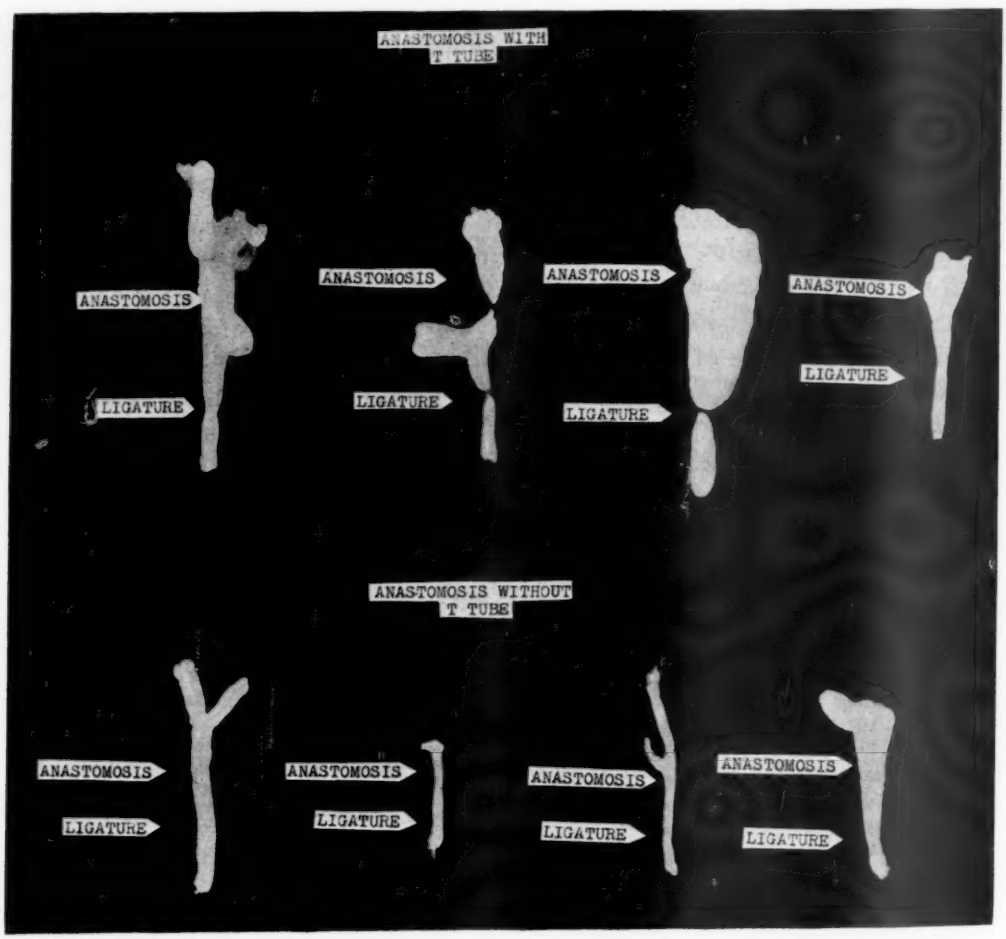
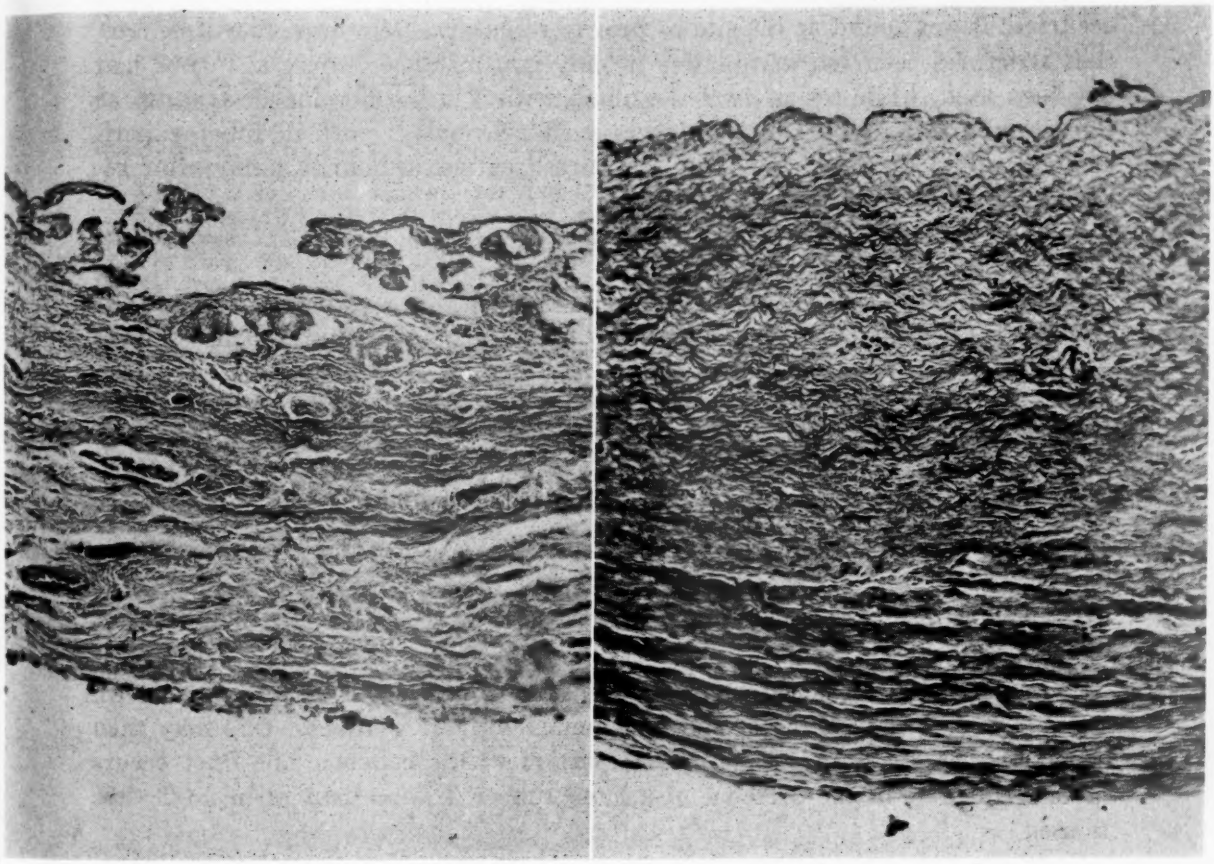


Fig. 2.—Demonstrative paraffin casts of the internal configuration of bile ducts which have been transected and anastomosed with a T tube (top row) and without a T tube (bottom row).

between the type of operation performed and stricture formation. Douglass and associates,[21] in work on the undilated duct, found fewer strictures formed when the bile was partially or completely excluded from the site of anastomosis. However, in these animals, fewer strictures were found when no bile was diverted.



A. *B.*

Fig. 3.—*A*, Microscopic section of transected and anastomosed bile duct in which no T tube was placed. Few abnormalities are present.

B, Microscopic section of transected and anastomosed bile duct in which a T tube was placed. Fibrosis and leukocytic infiltration is evident.

Positive cultures were found in all animals with T tubes, and in nine of fifteen animals without T tubes. There was no relationship between the type of organism present, and the presence of stricture formation. Isolated bacteria may be found in Table III. Others[22, 23] have found a higher incidence of infected bile in the presence of stones and T tubes, and Elkeles and Mirizzi[23] report that bacterial infection of the common bile duct is always associated with infection of other parts of the biliary system. This, in turn, may account for the increased leukocytic infiltration around the portal triads in animals in which T tubes were used. Microscopic sections also showed greater thickening and more leukocytic infiltration in the walls of the common ducts in which a

T tube was placed (see Fig. 3). From these results one may conclude that in the dilated duct of a dog a rubber tube used as a splint actually results in more fibrosis than when no splint is used.

While this experiment was primarily designed to study stricture formation after biliary anastomosis, it will be noted that in most instances where stricture occurred, it was found at the site of previous ligation. However, it will be seen that strictures occurred at this site in only two instances where a T tube had not been used, while ten of twelve animals with T tubes developed stricture at the site of previous ligation. As mentioned previously, work of other experimenters would serve to show that stricture does not ordinarily occur after removal of a temporary constricting ligature.

SUMMARY

Strictures of the common bile duct continue to be a distressing surgical problem. In order to study the effect, if any, of rubber tubing on the etiology of this condition, two operations were performed on forty-four dogs. Dilation of the duct was achieved by simple ligation. This was followed in one week by transection and anastomosis of the duct with or without a splinting rubber T tube. A T tube was used in twenty dogs and no T tube was used in twenty-four dogs. Rubber tube drainage was instituted in twelve of the latter group.

There was an over-all mortality rate of 37 per cent, due primarily to bile peritonitis. Since this was far more frequent in animals where no method of external drainage was used, it would seem advisable to drain all common duct anastomoses.

In the group sacrificed, stricture occurred in eleven of twelve animals with T tubes and in only three of sixteen animals without T tubes. One may then conclude that stricture of an injured portion of the common bile duct occurs more frequently in the presence of a latex rubber T tube than when no T tube is used.

Microscopic sections demonstrated increased fibrosis and leukocytic reaction in the wall of common bile ducts in which a T tube had remained for two months.

Bacterial infection is more common in the presence of a T tube since positive cultures were obtained in all animals with T tubes and in only 56 per cent of the animals without T tubes.

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SYMPATHECTOMY FOR CARDIAC DECOMPENSATION AND CORONARY DISEASE

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THE conclusions and suggestions presented here are based on the results of over twenty years of experience in the treatment of angina pectoris by injections and operations on the sympathetic nerves.

For several years alcohol injections of D_1 to D_5 on the left side and occasionally on both sides were used exclusively. Twenty-two consecutive patients were injected without a death, and with excellent results in over 80 per cent of the patients. The twenty-third and twenty-fourth patients died as they were injected. I then turned to surgery, using Pentothal Sodium anesthesia.

There have now been twenty-eight consecutive cases without a single operative death or one that could be even remotely related to the surgical procedure.

Over 80 per cent of the patients obtained from 75 per cent to 100 per cent relief. The cases in which the results were not satisfactory were due in each instance to one of three factors: incorrect diagnosis, drug addiction, or sex. The results in women have not been very satisfactory.

After more than twenty years of treating angina pectoris, I rarely have cases referred by internists or cardiologists. This cannot be because of the results. The operation is not experimental; it is well established, and is being done by many surgeons all over the world. It is based on entirely sound anatomic and neurophysiologic bases. The results are excellent; the mortality is practically nil. *What more can be asked of any treatment for anything?*

There are a vast number of "cardiac cripples" forced to live inactive lives, in constant dread of their next anginal attack, carrying their little bottles of nitroglycerine wherever they go, and being frequently forced to call their doctors for injections of morphine when the nitroglycerine doesn't work. The realization that well over 60 per cent of these cardiac cripples can be returned to useful, normal life, and that another 20 per cent or more can have a severe case of disabling angina pectoris reduced to a mild one, makes the lack of wider acceptance of this method of treatment difficult to understand.

Somewhat over a year ago, I experienced an almost fatal coronary occlusion, making, fortunately, a complete recovery. However, I can state categorically that if I should develop angina or any other type of cardiac disability, I would waste no time in having my upper dorsal sympathetic chain excised.

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CARDIAC DECOMPENSATION

It was my experience in the treatment of angina pectoris that led to the application of sympathectomy in the treatment of cardiac decompensation. As far as I know, I am the first, and perhaps the only, surgeon to advocate sympathectomy in the treatment of cardiac decompensation. Many of the cases of angina pectoris had greater or lesser degrees of decompensation associated with the angina. Invariably this decompensation disappeared after the angina was successfully treated by alcohol injection or surgery.

I can enumerate three striking examples; in addition, there were several other similar cases in this group.

CASE 1.—The first case of angina pectoris was that of a 63-year-old man. The patient suffered typical anginal pain involving the precordium and left arm, due to coronary sclerosis. He was unable to walk up the five or six steps to the office without puffing and becoming very blue. At night, there was marked swelling of his ankles. Two weeks after alcohol injection of D_1 to D_5 on the left side, this man climbed several hundred feet down a precipitous mountain cliff and back up again. He proudly informed me that he did not get short of breath nor did he have any sense of constriction or discomfort. His ankles were no longer swollen at night. This man remained well, without recurrence, for many years before I lost track of him.

CASE 2.—A 69-year-old man, with severe angina pectoris confined to the left side, due to coronary sclerosis, was injected with alcohol at D_1 to D_5 on the left side and there was immediate relief of anginal pain. Eight months later the patient began to have severe pain substernally, in the neck, and down the right arm. He rapidly became decompensated. This man slept sitting in a chair; he had been unable to lie down for weeks. Both legs were tremendously swollen, and he had marked ascites. Even sitting in a chair he was cyanotic, his respirations were labored, and he had constant pain in his right chest, neck, and right arm. He was obviously *in extremis*. The family was informed that it was most unlikely that he could survive the injection, but they prevailed upon me to make the attempt. Much to my surprise, he did survive the procedure, and recovered rapidly. Without any further medication of any kind, the ascites and swelling of the legs rapidly melted away, and within two weeks he was back at work. There was complete relief of pain and no further evidence of decompensation. He walked a mile and a quarter to his office each morning and repeated the walk home each evening for a period of three years of "borrowed time." One evening on his way home he collapsed and died suddenly at his gateway, at the age of 73.

CASE 3.—This case finally opened my eyes to the tremendous possibilities of further application of sympathectomy. A man 59 years of age, who had been in the hospital for one year, had become decompensated following a coronary occlusion. During his stay in the hospital he had developed severe angina pectoris. He was markedly edematous in both lower extremities, and ascites necessitated frequent paracentesis with removal of a gallon or more of fluid every few days.

This man was referred for sympathectomy for the relief of his anginal pain. Neither the referring doctor nor I expected to accomplish anything other than the relief of the angina—and we would have been very well pleased with such a result. However, within a week after left anterior cervicodorsal sympathectomy of the stellate and the first three thoracic ganglia, this man was entirely well. The ascites and edema disappeared promptly, without any medication, and he had no more anginal pain. He was discharged from the hospital one week after operation. This was almost ten years ago. He is now 68 years old, lives a perfectly normal life, does what he pleases, has never had any real anginal pain, but has a sense of constriction if he overdoes—which is a very definite warning.

It would seem that very little need be said about the results in these three cases. In each instance pain was relieved and decompensation promptly corrected. There is only one valid explanation of these results, namely, that it is due to increased blood supply to the myocardium. This is accomplished in the same manner as in an extremity, namely, vasodilatation and an increased collateral circulation, producing increased blood supply to the cardiac musculature.

After the third case, the tremendous implications of these results struck me forcibly. Every effort was then made to interest medical colleagues in the possibilities of this type of treatment in cardiac decompensation, with little success. About the same time, by virtue of the exigencies of war, my time was fully occupied for the next five or six years. It has only been in the last two or three years that my interest has again been awakened.

I would like very much to be able to recite a list of twenty-five or thirty cases of cardiac decompensation treated in the manner proposed. However, I have had only three cases which, of course, are too few to allow very definite conclusions to be drawn.[1] However, to these three cases may be added the three cases of angina pectoris with decompensation already described, making a total of six cases. In all of these cases the results were most satisfactory.

CASE REPORTS—CARDIAC DECOMPENSATION

CASE 1.—W. T. H., a 59-year-old man, had been hypertensive for many years. At the time of examination, he was edematous in both lower extremities and had fluid in his abdomen. He had been chronically decompensated for two years, never enough to be absolutely bedridden, but was constantly short of breath, and his lower extremities and abdomen were swollen at night. This man presented a case of hypertensive coronary disease with decompensation.

Operation, performed Dec. 1, 1949, was a left cervicodorsal sympathetic ganglionectomy. An anterior approach was used, and the stellate through the third dorsal ganglia were removed.

The anesthetist was actually loathe to give the anesthetic, as the patient breathed with difficulty, even while sitting up, and the operation was done in the prone position. By the time surgical anesthesia was established, he was *in extremis*. Immediately after the sympathetic nerves were severed, the anesthetist reported a remarkable improvement in pulse, blood pressure, and respiration. By the time the patient left the operating room, all signs of cardiac embarrassment had disappeared.

The electrocardiogram taken before the operation showed marked involvement of the myocardium. Following the operation the patient made a rapid recovery. He lost a great deal of fluid every day, in spite of the fact that he was not on cardiac medication. The swelling disappeared rapidly, both in the abdomen and in the lower extremities. He was able to breathe much easier than he had before, and for the first time in years was able to lie flat in bed all night. He remained in the hospital only one week, and an electrocardiogram on the day he left the hospital showed an amazing improvement. Before operation, the voltage was very abnormal, whereas the postoperative electrocardiograph showed a normal voltage.

I had intended to operate upon the other side. However, he did so well following the operation on the left side that I felt further operation might not be necessary and allowed him to go home, with instructions to return in the event of more trouble.

This case was startling in many ways: the man's extremely bad condition on the operating table, the immediate improvement at the time of operation, the marked changes in the electrocardiograph, and the fact that his decompensation markedly improved without any further medication for the heart condition.

For several months he remained markedly improved as compared with his status preoperatively. He then began to have more trouble and was urged to return to have the other side operated upon. He promised several times to come back but did not. He developed cerebral complications with convulsions, and died some months ago. I feel confident that his life would have been prolonged considerably if both sides had been operated upon.

CASE 2.— Mrs. V. B. L., aged 59 years gave a history of having had decompensation chronically for about nine years, with marked swelling of the ankles at night, which was gone in the morning. She had been in the hospital for two weeks, on several occasions, usually on medication with Salyrgan and bed rest, which improved her condition. She compensated quite well, but decompensated very easily after she got up and around. She was seen by a cardiologist, who made a diagnosis of old, posterior coronary occlusion, with aortic regurgitation on a rheumatic basis, hypertension, and decompensation. These findings were borne out by preoperative electrocardiographic studies.

On July 17, 1950, a left dorsal sympathetic ganglionectomy was performed, using a posterior approach. A portion of the second and fourth ribs on the left side were removed, and the sympathetic trunk was cleared and severed between the inferior cervical and the first dorsal ganglia. The first four dorsal ganglia and the intervening trunk were removed after severing all rami. The evidence of decompensation and swelling of the extremities was not present at the time she left the hospital. Electrocardiographs taken eleven days postoperatively showed definite improvement.

This patient refused to have the other side operated upon. A report was received on her on Aug. 20, 1951. She was working at that time and apparently has had sufficient improvement to be able to work without decompensating as she did before.

CASE 3.—Mrs. E. K., aged 67 years, gave a history of having had rheumatic fever with cardiac involvement at the age of 14. The diagnosis on this case was chronic cardiac decompensation on a rheumatic basis. The patient's first real trouble had started about four years previous to this examination, when she began to have swelling of the ankles and shortness of breath. She then became chronically decompensated with fluid in the extremities and in the abdomen. A course of Salyrgan and bed rest would improve her for two or three months and then she would gradually get worse again. About four months before I saw her, she decompensated, and this time treatment was not as effective as it had been. There was marked edema of the extremities, ascites, and shortness of breath. A cardiograph taken elsewhere showed marked myocardial involvement.

On Dec. 1, 1950, a left dorsal sympathectomy was performed, using a posterior approach. Ganglia D_1 through D_5 were removed.

Postoperatively this patient showed marked improvement. The electrocardiograph still showed a great deal of trouble: auricular fibrillation, right bundle branch block, and myocardial impairment. Because of postoperative complications, convalescence was stormy and prolonged. It was felt that it would be wise to give her approximately six months' rest before operating upon the other side and, consequently, she also was discharged with only one side operated upon. She has improved so much, however, that she does not wish to have the other side operated upon. Both the patient and her referring doctor feel that she would have been dead long ago if the operation had not been performed. She gets along quite well with a little digitalis and an occasional injection of Salyrgan, is able to be up and around and to do her housework, and is very well pleased with the result of the operation.

None of these cases was of the type in which we feel that surgery will be most successful, namely, in younger individuals who have intermittent bouts of decompensation with good compensation in between. All of these were chronic cases of long standing, and undoubtedly all of them had irreversible pathologic changes. Nevertheless, in all three patients, improvement was effective enough so that their lives took on an entirely different aspect. It is felt that the results in the cases described are sufficiently good to warrant the assumption that given

the proper type of case, this treatment would be successful in a large percentage of cases. In the future it is planned that both sides will be operated upon during a single hospital stay.

I have never been able to understand why circulatory lesions of the heart should be treated any differently than circulatory lesions of the extremities. One must assume, at least in the presence of heart disease, that the sympathetic fibers to the cardiac blood vessels are vasoconstricting in their action, and that severing the proper sympathetic nerves will produce the maximum vasodilatation of which the cardiac vascular tree is capable, just exactly as one expects the same result in sympathectomy for vascular lesions of the extremities. Perhaps the reason for hesitation in treating the heart muscle in the same manner as other muscles are treated is because of its vital function and a natural fear of upsetting in any way the existing cardiac mechanism.

Regardless of what physiologists may have said in the past, the effect of interruption of vasomotor fibers to the cardiac blood supply is vasodilating rather than vasoconstricting, at least in the presence of myocardial disease. This being the case, why shouldn't vascular lesions of the heart be treated as vascular lesions of an extremity are treated? It is agreed that, where there is an element of vasoconstriction, sympathectomy is indicated in the treatment of vascular lesions of the extremity. It is further generally agreed that if any type of treatment offers hope of improvement of an extremity, sympathectomy is the most adequate. *Why not apply the same reasoning in the treatment of heart lesions?*

In the treatment of cardiac decompensation, I believe that time will prove that any patient whose condition is amenable to medical treatment and who can be compensated by medication and rest in bed, can have intermittent attacks of decompensation changed to no further attacks of decompensation by this procedure. I believe further that there are many cases of decompensation that are not amenable to medical management, which will be markedly improved to the point of adequate compensation by proper sympathectomy. It will take many years and many operations on various types of patients to determine exactly which types are amenable to surgical treatment and, conversely, which have myocardial damage that is beyond help and which surgical treatment is of no value.

CORONARY DISEASE AND OCCLUSION

We now come to what is to me the most startling thought of all. Having recently had a personal experience with coronary occlusion, its onset, development, and consequences, I have come to some conclusions concerning the treatment of acute coronary occlusion. What I shall now present is largely speculative.

Here, again, the question comes up as to why we do not treat the heart as we treat an extremity, or even, let us say, as we have recently been treating thrombotic vascular lesions of the brain, namely, by injection or surgery of the sympathetic ganglia.

There are, of course, many factors involved in the production of coronary occlusion. First of all, it is apparently true in many cases, and certainly was

true in my case, that the original process at the onset was purely one of coronary vasospasm. In my own case, I would estimate it took thirty or forty minutes from the time of the onset of the painful coronary vasospasm until definite occlusion occurred. I feel quite sure that if it had been possible to have injected the sympathetic nerves early in that period of vasospasm, the massive coronary occlusion might have been avoided.

It is a well-known fact that where there is a sudden thrombosis or occlusion of any major blood vessel the entire vascular tree beyond that occlusion goes into vasospasm. If this vasospasm can be relieved before the circulation has been cut off for a sufficient period of time to cause death of the tissue, the resulting gangrene or infarction can be avoided. Proceeding further with this thought, it is reasonable to assume that the consequences of a coronary occlusion can perhaps, therefore, be changed from very serious ones to relatively minor ones. If there has occurred a considerable degree of occlusion and myocardial infarction, repeated injections or, better yet, sympathetic surgery should, in my opinion, provide a very rapid increase in collateral circulation by releasing vasospasm and, consequently, much more rapid healing of the myocardial lesions should take place.

I am, therefore, recommending that coronary occlusions be treated by immediate and repeated sympathetic injections and, probably, in many cases, sympathetic surgery after the acute phases of the attack have subsided. There is little doubt in my mind that the number of cardiac cripples due to coronary occlusion can be greatly reduced by this treatment.

It is also suggested that if a patient has had a coronary thrombosis and has had his prescribed period of rest, and still continues to have angina pectoris or evidence of cardiac insufficiency, or is in any way a cardiac cripple, that one should not hesitate to perform sympathectomy. The risk is practically nil. The results, I believe, will be spectacular.

In a recent survey of 1,700 cases of angina pectoris and coronary occlusion, Sigler[2] found that the average time that elapsed from the first symptoms of angina until the first coronary occlusion was less than three years. This being the case, it should not seem fantastic to visualize the day when, following the onset of angina pectoris, when it becomes apparent that a man is faced with the probability of continued anginal attacks and subsequent coronary occlusion, we will do prophylactic operations to alleviate angina and avoid coronary occlusion.

SUMMARY AND CONCLUSIONS

Excellent results are reported in over 80 per cent of fifty-two cases of angina pectoris treated in twenty-four instances by alcohol injection and in twenty-eight by sympathetic surgery.

Three cases of angina pectoris with associated cardiac decompensation were relieved of both angina and decompensation by sympathetic surgery.

Three cases of cardiac decompensation were markedly relieved by unilateral sympathectomy. It is felt that bilateral operation will be even more effective.

It is concluded that the ideal treatment for angina pectoris is sympathectomy.

Many cases of cardiac decompensation can be markedly improved by sympathectomy. Some of them can be virtually cured for many years.

The suggestion is made that coronary disease be treated by sympathetic injections in acute phases and surgery in chronic anginal states.

It is felt that sympathetic surgery will be effective as a prophylactic in preventing coronary occlusion.

It is suggested that sympathectomy preceding valvulotomy for mitral stenosis would greatly improve the result and in some cases might avoid the necessity of valvulotomy.

ADDENDUM

Since this paper was presented, three additional cases of decompensation have been operated upon. In all three instances the upper dorsal chain, D_1 through D_5 has been removed on both sides. The results have far exceeded my expectations. One case is particularly outstanding—that of a 69-year-old man who was hypertensive, and had a tremendously enlarged heart, bundle branch block, and auricular fibrillation. He had been decompensated and bedridden for months. At his age and with his findings I did not feel that I could accomplish anything, but he insisted, saying "I am no good as I am." The result has been amazing. At this writing, this man is living a normal life comparable to that of most men of his age.

In the most recent case, I used a superior, new surgical technique through a midline approach by way of transverse processes $D_{2, 3, 4}$ bilaterally, approaching the sympathetic trunks directly and removing both chains D_1 through D_5 in one stage with great facility. This new technique will be described in detail in another communication.[3]

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FURTHER OBSERVATIONS ON EXPERIMENTAL EXTRACORPOREAL CIRCULATION

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THE purpose of this report is to record the results of further investigation of a type of extracorporeal circulation employing a biological oxygenator previously described by Mustard and Chute.[1]

In this attempt to obtain a direct vision intracardiac approach, an extracorporeal circulation has been used which employs a circulation outside the body, substituting for the function of the individual's heart; yet the entire circulation of the individual is maintained. The advantage of replacing the function of both sides of the heart, rather than just one side as done by other observers,[2-5] is essential in considering interauricular or interventricular septal defects.

In connecting this mechanism to the animal, vessels are used which experience has shown may be ligated with impunity in the human being. The inferior vena cava is drained by way of the femoral veins, the superior vena cava by way of the azygos vein, and the blood is returned to the aorta by way of the right subclavian artery. At the onset of perfusion, the venae cavae are temporarily occluded at their entrance to the heart. This results in all the venous blood from the animal passing to the circuit where it is oxygenated. It is then returned to the animal's aorta by way of the femoral artery, where it is directed against the closed aortic valves. It then passes to all branches of the aorta, including the coronaries, so that the entire body is supplied with well-oxygenated blood under normal pressures. The entire circulation of the animal is maintained, yet the heart is empty of blood, aside from that which comes from the coronary circulation.

THE MECHANICAL HEART OR PUMPING SYSTEM

For the series of right auricular and right ventricular cardiotomies to be reported here, a pump mechanism designed by Campbell Cowan was used.[6] After previous experiments with De Bakey[7] and Dale and Schuster[8] pumps, we found the Cowan pump the best mechanism to replace the function of an animal's heart in pumping blood to all parts of the body under normal pressures (Fig. 1).

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This pump has an adequate output and is easily regulated by hand control. It allows easy sterilization; the pump units can be lifted out and autoclaved in one piece. There are no internal valves and hemolysis is negligible.

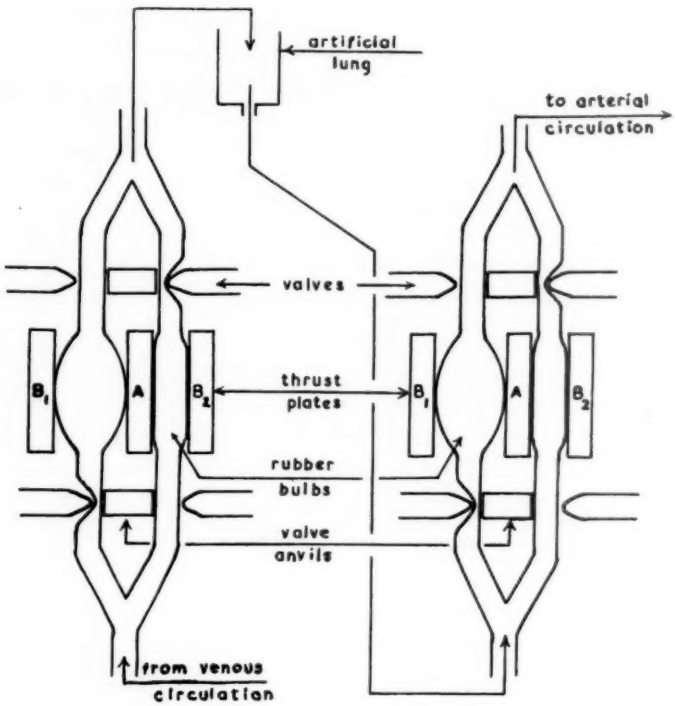

Fig. 1.—Artificial heart-lung circuit.

THE OXYGENATOR

Early in our search for an artificial lung we turned to a biologic oxygenator. Aside from the experimental failure of mechanical oxygenators in our hands, there were certain general considerations which indicated a biologic oxygenator offered the best chance of success. First, the lung tissue is an excellent oxygenator. It allows a massive surface area of blood for gaseous exchange in a normal environment, and with no undue trauma to the blood constituents themselves. Second, the lung is a first-rate filter, and in any extracorporeal shunt this filtering capacity becomes even more vital.[9] Third, most physiologists agree that the lung is more than just a mechanical oxygenator. It is thought that it carries out certain detoxification functions which are not clearly understood at this time. If portions of cardiac muscle, kidney, brain, or other tissues are perfused with oxygenated blood alone, the survival time is a matter of a few minutes. If, however, a portion of lung tissue is incorporated into the circuit, even though the lung is not utilized to oxygenate the perfusion fluid, the perfused material continues to survive for hours or even days, until infection or some other factor sets in. This would seem to indicate an essential lung function, aside from its ability to affect gaseous exchange.

Previously[1] the use of an animal's own lung as the oxygenator in the extracorporeal circulation was mentioned. There were numerous technical difficulties and the procedure necessitated a preliminary lobectomy.

The use of a lung from another animal of the same species was found to be the experimental method of choice. This is a very satisfactory procedure in dogs. For animals of similar weights, when using 100 per cent oxygen for inhalation, only one lobe is needed to effectively oxygenate the blood. It has been found that this lung tissue may be used up to 5 hours post mortem with real success, and varying periods beyond that time with decreasing success. In the cases to be reported here, lung tissue from one dog was used to maintain another on extracorporeal circulation.

REMAINDER OF THE EXTRACORPOREAL SYSTEM

In the remainder of the extracorporeal circulation there is included a bubble trap to safeguard against air embolism, and a water bath to maintain the perfusing blood at body temperature. All the tubing is of plastic material and the connections are glass. The entire inner surface of the extracorporeal system is coated with an organic silicone.[10]

HEPARINIZATION

In carrying out this work, there is a considerable problem in the control of blood coagulability from the following standpoints: First, the entire circulation of the animal is passed through a mechanical circuit outside the body, and is then returned to the animal. The fluidity of the blood in this extracorporeal circulation must be maintained. Second, the chambers of the heart are being opened and closed. The blood's coagulability must be accurately decreased to prevent the formation of a thrombus along the incision line. Third, the animal must not be allowed to die from hemorrhage at his multiple incision sites due to excess heparin dosage.

Aqueous heparin in the dosage of 10 mg. per 1,000 c.c. is added to the blood in the extracorporeal circulation, and 8 to 10 mg. are given intravenously (varying with the 10 to 15 kilogram size of the animal) at the onset of the operation. These dosages have been found to be adequate and safe with fairly long experimentation.

For postoperative heparinization a prolonged-action form of heparin has been used. The advantages of this in animal administration are obvious. The product used is a commercial one of sodium heparin dissolved in an aqueous vehicle containing gelatin and dextrose combined with vasoconstrictor substances.

In an effort to standardize dosage, experiments were carried out administering this substance subcutaneously and studying the results both by clotting-time method, and measure of blood heparin.

From the study of the apparent effects on clotting time, it is concluded that approximately 4 to 5 mg. of heparin per kilogram of body weight are required

TABLE I. THE RESULTS OF THIRTEEN CONSECUTIVE CARDIOTOMIES

DOG NUMBER	WEIGHT (KG.)	SITE AND LENGTH OF INCISION	SURVIVAL TIME	CAUSE OF DEATH	POST-MORTEM FINDINGS	POST-MORTEM AGE OF OXYGENATOR (MINUTES)	PERFUSION TIME (MINUTES)
1	16	Right auricle, 2 cm.	6½ months	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	175	18
2	16	Right auricle, 2.5 cm.	12 weeks	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	110	18
3	12	Right auricle, 2.5 cm.	5 months	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	95	25
4	12	Right ventricle, 3.0 cm.	10 days	Sacrificed	Incision well healed; no evidence of thrombus; pericardium mildly adherent	193	23
5	15	Right ventricle, 5 to 6 cm.	4 months	Sacrificed	Heart normal in size; incision well healed; no evidence of thrombus	203	26
6	11.6	Right ventricle, 4.0 cm.	36 hours	Prolonged hypotension	55 c.c. of bloody fluid in right chest, 115 c.c. in left chest; no thrombosis	227	26
7	13.5	Right ventricle, 3.0 cm.	4 months	Sacrificed	Heart normal in size; incision well healed; no evidence of thrombus	228	14
8	24.5	Right ventricle, 2.5 cm.	10 minutes	Air embolism	Tubing ruptured; gross air embolism	250	20
9	13.6	Right ventricle, 2.5 cm.	4 months	Sacrificed	Incision well healed; heart size normal; no evidence of thrombus	268	16
10	18.1	Right ventricle, 2.5 cm.	4 months	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	233	13
11	15.9	Right ventricle, 2.0 cm.	3 months	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	115	21
12	11	Right ventricle, 3.0 cm.	28 minutes	Air embolism	Blood reservoir empty; gross air embolism	210	25
13	14	Right ventricle, 2.5 cm.	4 months	Sacrificed	Incision well healed; no evidence of thrombus; heart size normal	277	42

over the course of twenty-four hours to maintain blood coagulability at two to three times the normal level. It has been shown that this level of clotting time is sufficient to prevent thrombosis in traumatized peripheral vessels. It would then appear sufficient for an incised heart with its rapid circulation. It has been shown that following extensive intimal trauma to blood vessels, thrombosis is prevented by adequate doses of heparin administered for approximately seventy hours.[11] In our work this time limit is exceeded to allow a safety margin, and therapy is maintained from four to five days postoperatively.

Fig. 2.—The heart of Dog 4 examined ten days postoperatively, showing no evidence of thrombosis formation.

EXPERIMENTAL RESULTS

Using this type of extracorporeal circulation, seventy-six experiments have now been performed in animals ranging from 7 to 24.5 kilograms in weight. In these experiments the entire circulation of the body was maintained for periods varying from nine to forty-seven minutes in duration.

These experiments have allowed direct vision intracardiac surgery with the performance of cardiotomy of the right auricle, the right ventricle, and the left ventricle. Interauricular and interventricular septal defects have been created and repaired, and procedures have been carried out on the mitral and pulmonary valves under direct vision.

In all cases the blood pressure was followed with a mercury manometer by direct femoral or carotid artery cannulization. The blood pressure was then kept at normal levels by regulation of the pump.

The results of four consecutive right auricular cardiotomies and ten consecutive right ventricular cardiotomies are shown in Table I. The right auricle was opened for an average distance of 2.2 cm. in three cases and was closed with no fatalities.

In ten consecutive cases the right ventricle was opened for an average distance of 3.2 cm., the incisions varying from 2 to 6 cm. in length. In this group three deaths occurred, one of which seemed unavoidable. The dog died thirty-six hours postoperatively because difficulty was encountered in removing the venous clamps at the termination of perfusion, and a prolonged period of hypotension with anoxia resulted. Dog 12 died of air embolism due to an insufficient amount of blood in the venous reservoir. Dog 8 died of air embolism due to puncture of one of the latex tubes at the valve sites.

Fig. 3.

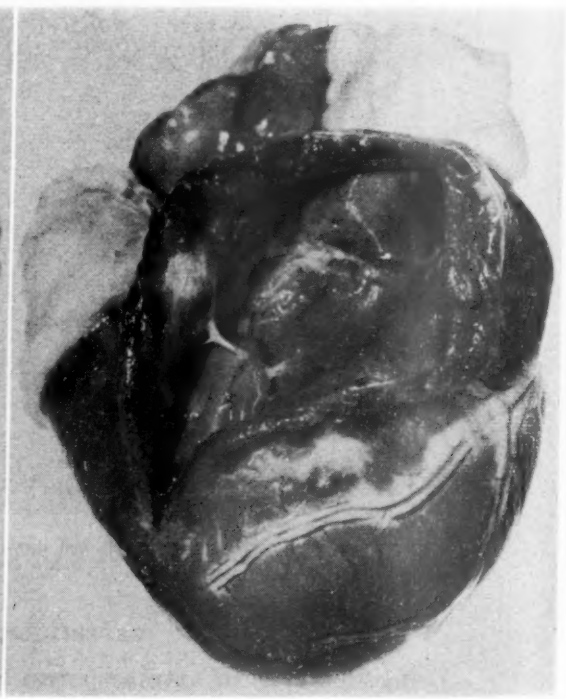

Fig. 4.

Fig. 3.—The heart of Dog 10 examined four months postoperatively, showing well-healed right ventricular cardiotomy. Note adherent pericardium.

Fig. 4.—The interior of the heart from Dog 10 examined four months postoperatively, showing well-healed scar covered with endocardium.

DISCUSSION

In the series of right ventricular cardiotomies adequate exposure was obtained of the interventricular septum, and digital as well as visual examination

of the pulmonary conus and valves was allowed. This exposure appeared sufficient for a case of interventricular septal defect or pulmonary infundibular stenosis.

Fig. 2 is the heart of Dog 4 examined ten days postoperatively, showing no evidence of thrombosis formation. All of the remaining dogs were allowed to survive four or more months postoperatively. When sacrificed these animals showed normal hearts, aside from well-healed incisional sites. Figs. 3 and 4 show typical findings.

The healing of the ventricular wound is by scar tissue and, as shown, the area of scar produced is not unlike a healed cardiac infarct. It is apparent that such a scarred area should not be placed in the left ventricle with its high pressures, but that the safer approach is through the right ventricle.

In repairing the cardiac incision, a continuous everting mattress suture of arterial silk has been used, followed by a continuous running superficial silk suture. The suture is carried deep into the cardiac muscle but caution is taken not to go through the endocardium, as it is desired that no foreign matter should appear on the endocardial surface.

From our work it appears that the use of another dog's lung tissue allows safe cardiotomy on the experimental animal. Where cardiotomy alone is performed the survival rate is good. When artificial defects have been created in an effort to later repair them, the survival rate has not been good due to the abnormal cardiac function created.

The possibilities of applying this principle of a biological oxygenator to human beings are now being investigated through the study of human lungs obtained at autopsy and operation, and the study of lungs of other species.

SUMMARY

1. The principles of an extracorporeal circulation employing a biologic oxygenator are stated.

2. The merits of a biologic oxygenator are reviewed and its experimental use is reported.

3. The problem of heparinization in extracorporeal circulation with successful cardiotomy is considered.

4. The experimental results of three consecutive auricular cardiotomies and ten consecutive right ventricular cardiotomies are given.

5. The possibilities of applying the principle of a biologic oxygenator to human beings are mentioned.

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ADRENOCORTICAL FUNCTION DURING SURGICAL PROCEDURES

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THE prompt peripheral utilization of adrenocortical hormones is evident from failure to detect them in the peripheral blood of experimental animals even when the liver or the liver and the kidneys have been removed.[29] The very small quantities of hormone excreted in the urine of man under optimal or stressful conditions lend further support to this contention. A rough estimate of the daily output of the normal adrenal cortex is obtained from the fact that the absorption of 5 mg. of cortisone per day partially restores to normal the metabolic aberrations of a patient with Addison's disease.[10] In disease or during muscular activity, however, the excretion of urinary corticoids may increase remarkably; this amount represents a very small fraction of the quantities of hormones required to maintain eucorticism in adrenalectomized animals[14] or in patients with Addison's disease[27] exposed to comparable degrees of stress. The conclusion appears inescapable that the adrenocortical steroids undergo rapid change in the tissue, but the nature of this change is unknown.

There is no doubt now that the discharge of adrenocorticotropic hormone from the adenohypophysis which activates the adrenal cortex is an essential link in a series of metabolic and functional alterations, initiated by any stress. Since atrophy of the adrenal cortex is consequent to hypophysectomy,[7] stress, which normally increases the size and decreases the concentrations of sudanophilic substance, cholesterol, and ascorbic acid in the adrenal cortex fails to influence this gland in the absence of the pituitary.[13, 23] The adrenocortex of the hypophysectomized animal is unresponsive to stress; the gland undoubtedly continues to secrete adrenocortical hormone, but in minute quantities and at a constant rate. The important role of the adenohypophysis in response to stress is indicated by the sensitivity of hypophysectomized animals to a variety of nonspecific stresses[4, 5, 15, 18, 20, 28] and the fact that adrenocortical extract increases the resistance of such animals to the stress of cold.[4, 28]

Among other changes, it has been well established that the circulating blood level of the C-11, 17 oxygenated steroids is reflected by the number of eosinophils circulating in the blood stream.[3, 6, 8, 9, 11] In man, failure to demonstrate an eosinopenia following the administration of adrenocorticotropic hormone is evidence of adrenocortical insufficiency[26] and if eosinopenia does not follow operation, failure of the adrenocortex should be suspected.[21] Evidence is accumulating that the eosinophil test will detect even relative adrenocortical insufficiency, at least in experimental animals.[25]

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Despite the lack of clear-cut information defining the exact manner of adrenocortical hormone utilization during stress, certain broad aspects of the problem are worthy of consideration. In general, it would appear that the rate of adrenocortical hormone utilization parallels cellular activity and that the hormone is necessary for the mobilization of energy for cellular work. For example, eosinophil counts indicate that the adrenocortex is hypoactive in myxedema,[16] and that thyroidectomy is followed by adrenocortical atrophy in animals.[17] On the other hand, the adrenocortex is hyperactive in hyperthyroidism.[12, 16, 30] These facts are compatible with the thesis that adrenocortical hormone utilization parallels cellular activity and that the increased cellular activity which accompanies homeostatic adjustments to stress may be responsible at least in part for the parallel increase in the rate of utilization of adrenocortical hormone.[24]

It has been demonstrated clinically that in hypopituitarism with adrenal insufficiency a surgical procedure is poorly tolerated before, and well tolerated after, preliminary priming therapy with adrenocorticotropic hormone.[22] If, however, similar patients were prepared presumably to an adequate degree for a surgical procedure with cortisone acetate, additional information concerning the relative rate of utilization of the steroid and absolute adequacy of preparation could be determined.

MATERIAL AND METHODS

Three major groups of patients were employed in this investigation. Two patients with chromophobic adenoma tumors of the pituitary gland made up one group. The second group was composed of two types of cases; ten patients selected at random, each of whom underwent a major abdominal surgical procedure and presumably were endocrinologically normal, and two cases, selected (after completion of the study) because of the similarity of the surgical procedures and preoperative examination, and the contrasting results. The third group contained one patient who received testosterone propionate before operation, a dose of 50 mg. per day.

Control preoperative examination for all patients studied consisted of the epinephrine-eosinophil test to determine the relative responsiveness of the entire pituitary-adrenocortical axis. The test dose of epinephrine was 0.3 c.c. of a 1:1000 dilution injected subcutaneously. Examinations were made in the postabsorptive state and the control eosinophil count was taken immediately preceding, and the second count exactly four hours after, the epinephrine injection. The cell counts were made in a Levy chamber according to the method recommended by Randolph and Rollins.[19] For the definitive study, following a control count taken just prior to the induction of anesthesia, frequent serial eosinophil counts were made throughout the period of anesthesia and of operation. The counts were recorded as percentage changes from the control level in the second and third groups of patients; in the first group of patients they were recorded as percentage changes from an average of counts taken before preoperative preparation with cortisone acetate.

RESULTS

In the two groups of general surgical cases, the patients demonstrated a satisfactory preoperative response to the epinephrine-eosinophil test as shown in Figs. 1 and 2. In Fig. 1, the mean percentage change in circulating eosinophils after 0.3 c.c. of epinephrine for the ten random surgical cases is –82.5 per cent. Fig. 2 shows test results of –81 per cent and –87 per cent for each of two patients in the same age range with diagnoses of cardioesophageal carcinoma, for whom resection was planned through a thoracoabdominal incision. In all respects, the latter two cases were as identical as could be desired for the comparison of results to follow.

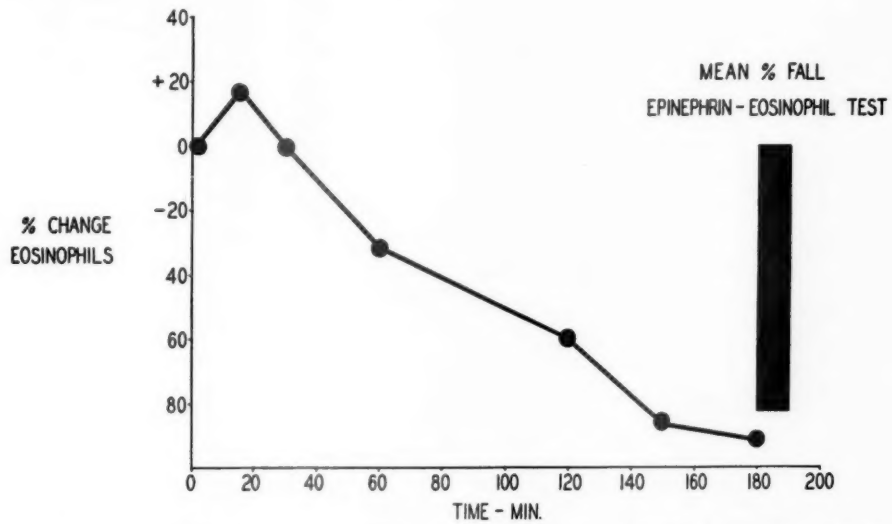

Fig. 1.—Graph of mean values obtained from study of 10 endocrinologically normal patients. The bar indicates the mean eosinophil fall after epinephrine as determined before operation. The line graph indicates the average pattern of eosinophil fall during the course of anesthesia and operation.

In contrast was the preoperative evaluation of the pituitary cases with epinephrine-eosinophil responses of –23 per cent and –21.5 per cent, respectively, indicating a relative pituitary-adrenal insufficiency (Fig. 3). At no time did either of these two patients give evidence to suggest the existence of a diabetes insipidus state. Both of these patients were prepared for operation by four daily intramuscular injections of 100 mg. of cortisone acetate. Two hours before operation, each received intramuscular injections of 50 mg. of cortisone acetate at two different sites. The control eosinophil counts just before induction of anesthesia were –85 per cent and –80 per cent of the pretreatment levels, well within the range of an adequate response to epinephrine in the normal patients (Figs. 1 and 3). The single patient of group three showed a good response in the epinephrine-eosinophil test prior to treatment with testosterone but was not retested after receiving this steroid preoperatively.

Fig. 1 shows the pattern of mean relative changes in circulating eosinophils during the course of operation on ten major abdominal cases selected at random. After an initial eosinophilia, there is a rapid progressive fall in eosinophils,

indicating a progressively increasing production of adrenocortical secretion. Fig. 3 shows the individual records of circulating eosinophil changes during the course of operation in each of the two pituitary cases. Case 1 (solid circles) had a two-peaked elevation in the number of cells, neither of which peaks

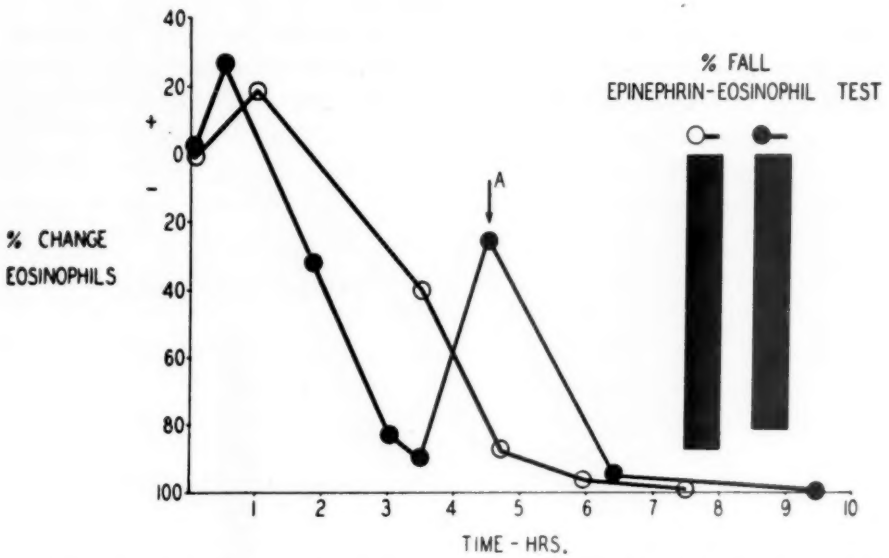

Fig. 2.—Bar graphs show results of preoperative epinephrine-eosinophil test in 2 presumably endocrinologically normal cases. Line graphs demonstrate serial eosinophil counts during the course of the operation on each (see text for details).

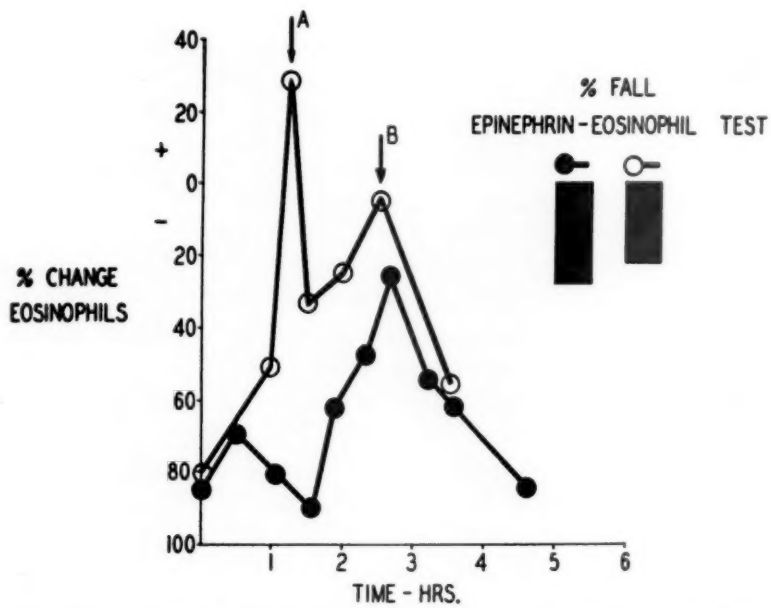

Fig. 3.—Two primary panhypopituitarism cases. Bar graphs show preoperative eosinophil response to epinephrine. Preoperative preparation was with cortisone acetate. Line graphs indicate percentage changes in eosinophils during course of operation (see text for details).

exceeded –25 per cent. At each of these points the intravenous rate of infusion of whole adrenocortical extract was increased with subsequent prompt fall in the eosinophil count. The course of the operation was completely uneventful, as judged from the anesthesia record. Case 2 (open circles), on the other hand, presented some remarkable deviations. At point *A* in Fig. 3, the patient's mean blood pressure fell to 60 mm. Hg and the eosinophil count rose to plus 28 per cent; the prompt intravenous administration of 100 c.c. of whole adrenocortical extract immediately returned the blood pressure to a normal of 110 mm. Hg and the eosinophil count to a level within the expected trend. At point *B*, however, the patient had a sudden blood loss estimated at 1,000 c.c. and the mean blood pressure fell to 0 mm. Hg with an eosinophil count of plus 5 per cent. Prompt blood transfusion and 100 c.c. of adrenocortical extract intravenously again improved the clinical condition with a prompt fall of the eosinophil count to –55 per cent.

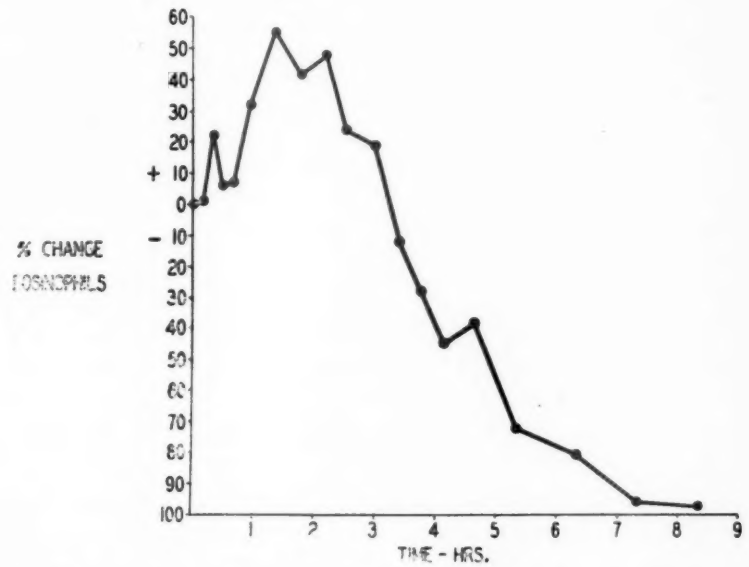

Fig. 4.—Line graph showing pattern of eosinophil fall during the course of an operation on a patient who had received testosterone propionate for one week prior to operation.

Fig. 2 constrasts the clinical course during operation of the two very closely comparable general surgical cases. Case 3 (open circles) followed the anticipated pattern as shown in Fig. 1; the clinical course was completely uneventful, again as recorded on the anesthesia chart. In contrast, Case 4 (closed circles) was subjected to a sudden blood loss estimated at 500 c.c. just prior to the time indicated by point *A* at which time the eosinophil count had risen suddenly from –90 per cent to –25 per cent. At this time the mean blood pressure was 55 mm. Hg. No adrenocortical extract was given but it required the rapid administration of 1,500 c.c. of blood to stabilize the blood pressure and the eosinophil count. The results in the single case which represents group three are presented in Fig. 4. Experimental studies suggest that the protein

anabolic or anticatabolic effect of testosterone is due to its effect of blocking the pituitary release of adrenocorticotropic hormone.[1, 2] By the preliminary treatment with testosterone a condition of relative pituitary adrenocortical insufficiency was produced as illustrated. In this case satisfactory clinical and experimental response to the stress of anesthesia and surgery as reflected in the anesthesia record and the eosinophil count was not attained until a period of 5½ hours after the initiation of the stress. This compares unfavorably with the group of control cases shown in Fig. 1 who attained the same level of adrenocortical response to the pituitary release of adrenocorticotropic hormone in a little over two hours. In percentage evaluation the patient given testosterone was adrenocortically more insufficient than either of the pituitary patients of Fig. 3 who had been prepared with cortisone acetate.

DISCUSSION

The preoperative preparation of the patient with a relative pituitary-adrenal insufficiency by means of minimally soluble cortisone acetate provided an opportunity to appraise the organism's requirements for adrenocortical steroids during the stress of a surgical procedure. The supply of the injected steroid to the body was determined entirely by its relative solubility in tissue fluids. On this basis, the steroid release was uniformly constant and of sufficient magnitude to reduce the control preoperative eosinophil count to a level of satisfactory clinical significance. Such a supply, however, in no way satisfied the body requirements for the steroid as the anesthesia and operation progressed, because both pituitary cases showed rises in cell counts at the same time the normally responding pituitary-adrenocortical axes of the control general surgical cases were demonstrating progressive falls in eosinophils (Figs. 1 and 3). Although no quantitative information is possible, qualitative deductions reveal that body processes under stress require enormously large supplies of adrenocortical steroids to provide the usual pattern or response, as judged by the eosinophil response.

It is interesting that a sudden blood loss, as in Case 4, Fig. 2, produces a temporary state of relative adrenocortical insufficiency, with clinical changes amenable only to overreplacement of the estimated blood loss. Whole adrenocortical extract might be a useful adjunct in such a situation if there were assurance that an adrenocortical insufficiency is playing a role in the clinical picture.

The preoperative administration of testosterone propionate induces a delay in the response of the pituitary-adrenocortical axis to stress. In this way such a case may closely simulate cases in surgical practice with unrecognized minor degrees of hypopituitarism or hypoadrenocorticism.

SUMMARY

The greatly augmented requirements of the organism for adrenocortical steroids during stress have been qualitatively demonstrated. That these requirements may exceed the ability of the pituitary-adrenocortical axis to produce them on occasions of either unrecognized pre-existing hypopituitarism or

of sharp accentuations in the severity of the stress has been shown. These conditions can be avoided by the more frequent employment of the epinephrine-eosinophil test as part of the preoperative evaluation of patients and also the adjunctive use of the eosinophil count during the course of a difficult and protracted surgical procedure. The justified and judicious use of aqueous adrenocortical extract might assume its proper orientation in the therapy of surgical shock when relative adrenocortical insufficiency has been demonstrated by the eosinophil count.

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CARBOHYDRATE METABOLISM IN THE IMMEDIATE POSTOPERATIVE PERIOD

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INTRODUCTION

THE adequate response of an organism to any stress requires the prompt activation of the pituitary-adrenocortical axis as a prerequisite to survival. Implicit in this mechanism is the release by the pituitary of endogenous adrenocorticotropic hormone and the consequent increase in production of adrenocortical steroids.

A state of metabolism similar in many respects to clinical diabetes mellitus with decreased carbohydrate tolerance has been produced in normal human beings[6] and a pre-existing diabetic state has been intensified[11] by the exogenous administration of adrenocorticotropic hormone; characteristically in these clinical studies, the diabetes was extremely resistant to insulin, a finding that has been confirmed in animals.[21] Whether this hyperglycemia is a matter of decreased peripheral utilization (as studied in animals)[22] or not (as studied in human subjects)[14] is still controversial. In fact, there are some who hold that adrenocortical extracts may enhance the peripheral utilization of carbohydrate.[26] Many responsible investigators have championed the view that there is no effect on peripheral utilization, basing their views on the relation of inorganic serum phosphate to carbohydrate metabolism since phosphate is "consumed" during the phosphorylation stage in the normal intermediary metabolism of carbohydrate, and so, during carbohydrate utilization, is manifested as a temporary decrease in the level of serum inorganic phosphorus.[8, 14, 16, 17, 28, 31, 34-36]

From this point of view, it seemed of interest to investigate carbohydrate metabolism in the immediate postoperative period, at a time when the bodily economy has been disturbed by the stress of an anesthetic and operation, since alterations in carbohydrate metabolism have been shown to occur within twenty-four hours after the administration of exogenous pituitary adrenocorticotropic hormone.[5]

MATERIALS AND METHODS

Twenty adult white male patients, between the ages of 30 and 60 years, in good nutrition and maintained on the standard hospital diet (70 Gm. protein, 300 Gm. carbohydrate, 2,400 calories) prior to the test, were selected for this investigation. Each of the patients was subjected to a major abdominal operation.

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TABLE I. DATA FROM NORMAL CASES STUDIED*

		FASTING	½ HR.	1 HR.	2 HR.	3 HR.	4 HR.	5 HR.	6 HR.
Preoperative	Glucose Mg. %	77 ±12	203 ±23	130 ±20	73±11	62± 8	71± 7	74± 6	75± 8
20 cases	Phosphorus Mg. %	3.3± 0.3	2.7± 0.2	3.4± 0.3	—	—	—	—	—
Postoperative						—			
10 cases	Glucose Mg. %	82 ±20	215 ±47	137 ±23	82±13	65±14	69±16	70±10	75± 9
ether	Phosphorus Mg. %	3.0± 0.2	2.5± 0.1	2.8± 0.3	—	—	—	—	—
10 cases no	Glucose Mg. %	82 ± 7	220 ±17	164 ±12	88±11	80± 9	75±10	78± 8	84± 9
ether	Phosphorus Mg. %	3.3± 0.4	2.8± 0.3	3.3± 0.2	—	—	—	—	—

*Preoperative glucose tolerance tests done on 20 cases; postoperative tests on 10 who received ether and on 10 who did not. Pertinent phosphorus levels also are shown. Values presented as mean ± one standard deviation.

The intravenous glucose tolerance test of Thorn and associates[39] was employed. The selection of it was based on the fact that the average rate of normal intestinal absorption of glucose equals 0.5 Gm. per kilogram of body weight per half hour in man. The additional advantages were that such a test avoided the misinterpretation of effects due to altered intestinal absorption and permitted the postoperative testing of patients in whom oral intakes were not allowed because of the nature of the surgical procedure. Glucose in a 20 per cent solution (0.5 Gm. per kilogram of body weight) was given intravenously

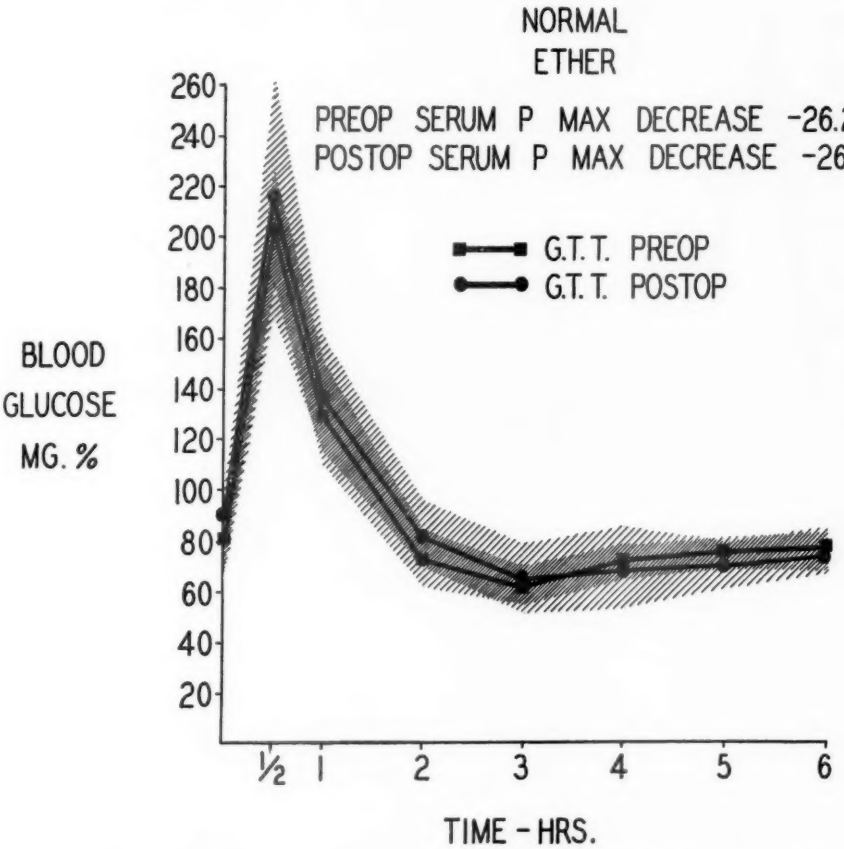

Fig. 1.—Glucose tolerance curves from normal patients who did receive an ether anesthetic. Twenty preoperative studies and ten postoperative. The cross-hatched area indicates a range of plus-minus 1 standard deviation from the mean. There is no significant difference between preoperative and postoperative glucose tolerance or serum inorganic phosphorus maximum decrease.

over a 30 minute period. A fasting venous blood sugar sample was drawn and blood sugars were determined at 30 minutes, and at hourly intervals, 1 through 6 hours following the completion of the infusion. Blood specimens for inorganic serum phosphorus were drawn simultaneously with those for sugar. Eosinophil counts were made according to the method of Randolph and Rollins[29] at the beginning and at the end of the test and averaged. The patients were all 12 hours postabsorptive when examined and the complete series of studies was done the day before and the day following an operation.

Blood glucose values were determined by Fister's modification of the Nelson-Somogyi method.[13] Serum inorganic phosphorus was measured according to the method of Fiske and Subbarow.[12]

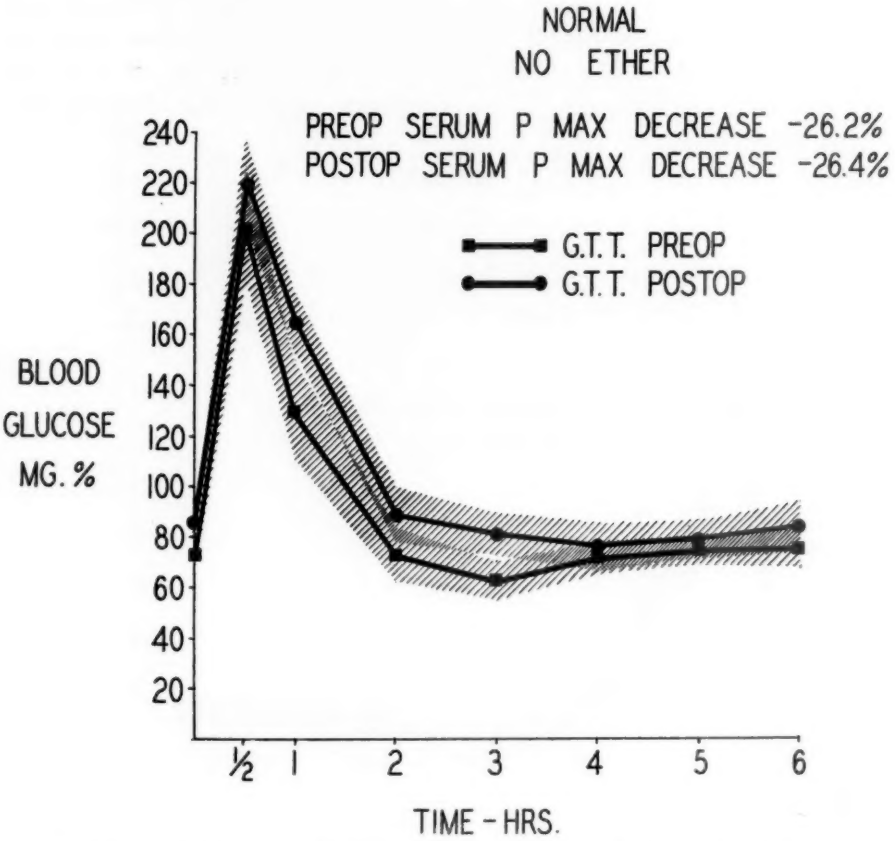

Fig. 2.—Glucose tolerance curves from normal patients who did not receive an ether anesthetic. Twenty preoperative studies and ten postoperative. The cross-hatched area indicates a range of plus-minus 1 standard deviation from the mean. There is a significant difference between preoperative and postoperative glucose tolerance but no significant difference in the serum inorganic phosphorus maximum decrease.

METHODS

As evaluated by comparison of the average postoperative eosinophil count with the average preoperative count, the pituitary-adrenocortical response was adequate in every case studied with a range in fall of –80 per cent to –100 per cent produced by the stress of the operative procedure. The pertinent data on carbohydrate metabolism obtained under these experimental conditions are presented in Table I. Preoperative values for the glucose tolerance test were well within the accepted limits of normal. The effect on glucose tolerance of operative trauma with its resultant increase in availability of adrenocortical steroids is apparent only when the postoperative data are examined with the added criterion of the type of anesthetic employed. If the cases which received ether as the anesthetic agent are considered as a separate group, no

significant difference in the values for the glucose tolerance test (Table I or the type of curve obtained (Fig. 1) occurs, and presumably this is due to the glycogenolytic action of the ether.[1, 10, 15, 27] If, however, the data from a contrasting group which received no ether are reviewed (Table I and Fig. 2) a statistically significant difference is present, with a decreased tolerance for glucose appearing. The apparent difference between the two groups in the postoperative tolerance is not due to changes in utilization of the carbohydrate but to the glycogen content of the liver at the time of the test.[4] Ether has effected a definite glycogenolysis and probably because of this glycogen depletion the glycogenic action of the adrenocortical steroids is reflected in a normal tolerance due to the rapid deposition of the blood glucose into the liver as glycogen. If, however, the liver is glycogen-rich, as was true with the subjects receiving no ether, the tolerance curve portrays more accurately the state of carbohydrate metabolism with an observable decreased tolerance.[4]

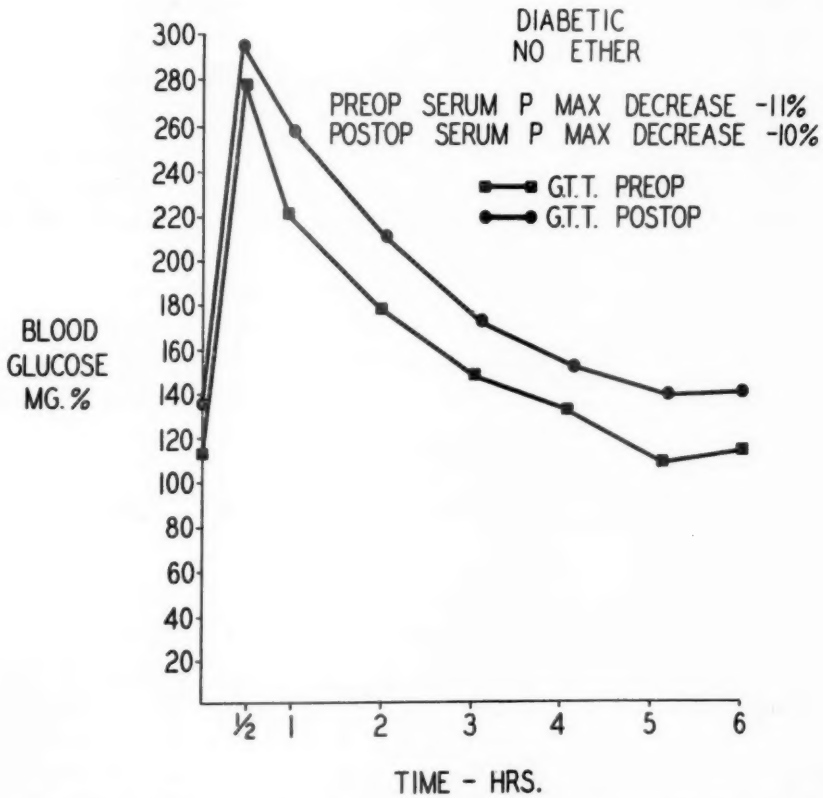

Fig. 3.—Single patient with diabetes mellitus who received no ether. There is decreased tolerance to carbohydrate postoperatively, but no significant change in serum inorganic phosphorus maximum fall (cf. Fig. 2).

In the preoperative examinations and in both anesthetic groups postoperatively, the mean maximal decrease in serum inorganic phosphorus was about 26 per cent, in agreement with the values obtained in normal subjects and those reported to occur under the influence of adrenocorticotropic hormone therapy.[14]

The uniform changes in phosphorus levels would indicate that the apparent decrease in carbohydrate tolerance occurring in the postoperative period as produced by the adrenocortical steroids is not due to decreased peripheral utilization but perhaps to a marked increase in gluconeogenesis.[24]

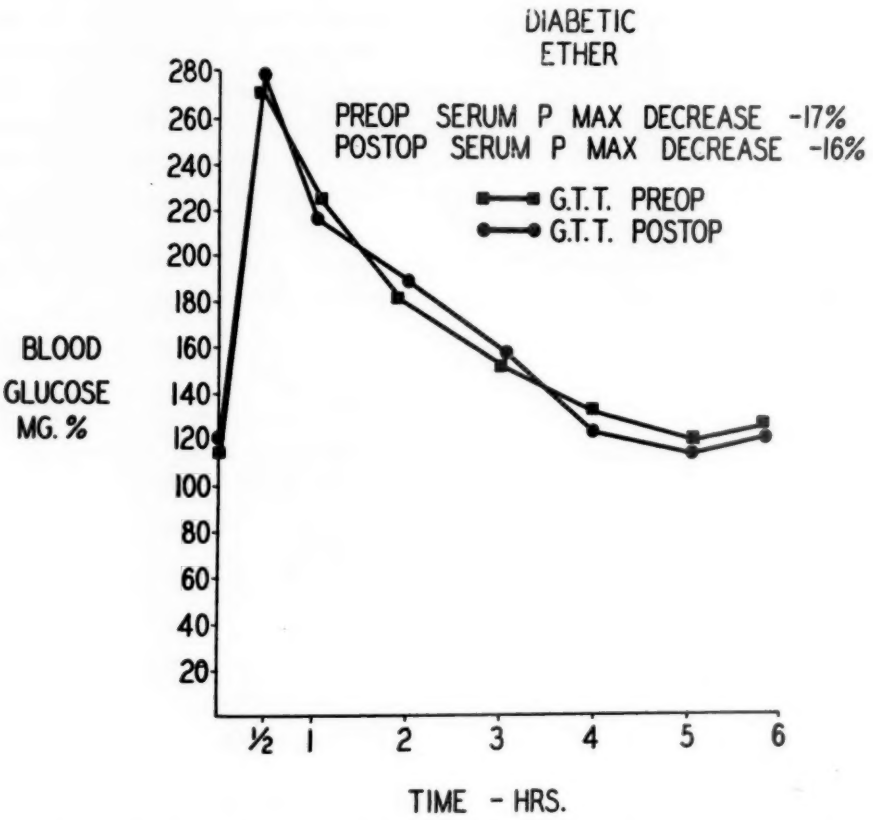

Fig. 4.—Single patient with diabetes mellitus who received an ether anesthetic. There is no difference in carbohydrate tolerance or serum inorganic phosphorus maximum fall in the postoperative study (cf. Fig. 1).

Further light is thrown on the problem when two cases studied apart from the above group are considered. Each of these cases had an established diagnosis of mild diabetes mellitus and was studied as the nondiabetic patients were, but with the added feature that all insulin had been withheld for the 24 hours preceding the time of testing. The preoperative intravenous glucose tolerance curves confirmed the diagnosis of diabetes mellitus by both the criterion of a decreased tolerance and that of less maximum decrease in serum inorganic phosphorus during the test, the latter values being –11 per cent and –17 per cent, respectively.[14] One patient was operated under ether anesthesia, the other was not. Fig. 3 shows the anticipated intensification of the diabetic state with a significant further decrease in carbohydrate tolerance, yet the change in serum inorganic phosphorus was not altered appreciably (–10 per cent); this patient had not received ether. Fig. 4 shows the postoperative tolerance curve from

the patient receiving ether with no significant alteration in either the carbohydrate tolerance or the serum inorganic phosphorus (−17 per cent preoperatively and −16 per cent postoperatively).

DISCUSSION

An integral part of the composite picture of metabolic alterations produced by surgical trauma is a decreased tolerance to glucose. Clinical recognition often has been given to this phenomenon[38] with descriptions of "postsurgical diabetes" and the establishment of the fact that true diabetes mellitus is intensified and becomes relatively resistant to insulin as a result of trauma, infection, or operation. With the advent of a new era of investigation made possible by the ready availability of adrenocortical extracts, steroids, and adrenocorticotropic hormone as investigative tools, and with the recent advances in the knowledge of the neuroendocrine physiology of stress,[20, 30, 32, 33] much informative light has been shed on what were previously metabolic puzzles. Direct comparisons now can be drawn between the metabolic effects of either exogenous or endogenous adrenocortical activation.

To the many metabolic phenomena that occur in the posttraumatic period such as nitrogen, potassium, sulfur, and phosphorus loss, and sodium and water retention,[2, 3, 7, 9, 18, 19, 23, 37] can be added that of a possible glycosuria and a certain hyperglycemia. The exact cause of this decreased carbohydrate tolerance in the postoperative period is not known exactly, but interpreted in the light of concurrent alterations in phosphorus metabolism probably is not due to any interference with peripheral utilization. It is exactly the same "abnormality" in carbohydrate metabolism that is seen both in Cushing's syndrome and during high-dosage therapy with adrenocorticotropic hormone or adrenocortical steroids. For this comparable reason it is classed as insulin resistant. Whether this decreased tolerance always can be demonstrated during the postoperative period depends to a large extent on the glycogen content of the liver[4] which in turn is determined by the type of anesthetic agent employed.

SUMMARY

During surgical convalescence, an insulin-resistant type of decreased carbohydrate tolerance occurs as a part of the metabolic response to trauma. Presumably, this decreased tolerance is not due to an interference with peripheral utilization.

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RELATIONSHIP OF THE LIVER TO THE SERUM NONSPECIFIC HYALURONIDASE INHIBITOR

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(From the Laboratory of Surgical Research, Department of Surgery, Western Reserve University)

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Certain noteworthy experiments have provided clues as to the in vivo site of production. Glick,[1] in 1948, demonstrated by means of electrophoretic fractionation that the inhibitor activity of human serum migrated chiefly with the albumin fraction. Likewise, in a group of patients with various types of liver disease, the inhibitor level was noted to rise in the serum, except in those cases in which the disease process was so far advanced as to result in complete hepatic failure, in which instances the titer fell to below normal levels.[2] These findings have led us to direct our attention toward the liver as a possible source of the nonspecific inhibitor. Wattenberg and Glick[3] attempted to demonstrate the inhibitor in tissue extracts of rabbit liver, lymph nodes, spleen, kidney, pancreas, brain, and lungs, but were unsuccessful.

A series of experiments has been performed in this laboratory to determine the source of the inhibitor in dogs by "organ exclusion" studies. Utilizing the knowledge that tissue trauma[4] and various systemic diseases and stress situations[5] result in an elevated titer of the hyaluronidase inhibitor, we reasoned that it might be possible to abort this response by removing, surgically, various organs from the systemic circulation and following the titer of the inhibitor during the postoperative period. This indirect approach has obvious limitations, but until further identification of the inhibitor is forthcoming, it may shed some light on the in vivo formation of the inhibitor.

METHOD

Healthy mongrel dogs were anesthetized with intravenous Nembutal and, under aseptic conditions, subjected to laparotomies. A so-called "physiologic hepatectomy" was performed on fourteen animals. This was accomplished

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*Dr. Edward Henderson of Schering Corporation, Bloomfield, N. J., generously supplied us with the hyaluronic acid and hyaluronidase used in these experiments.

by anastomosing the portal vein to the inferior vena cava and completely diverting the venous inflow of portal blood to the liver. The hepatic artery, as well as the entire gastrohepatic ligament, was then ligated, and any anomalous arterial branches noted at the liver hilus. In several of the experimental animals the common bile duct was also ligated, but there was no difference noted in the inhibitor level between these animals and the ones in which the bile duct was spared. Two types of control animals were employed. In one group consisting of two animals, the portal vein was anastomosed to the inferior vena cava in a fashion identical with that used in the experimental group; however, the hepatic artery was not ligated. These animals survived. Another group of six control animals underwent simple abdominal laparotomies and closure of the abdominal incision.

Blood samples for determination of the inhibitor were drawn from all animals preoperatively, at the completion of the operation, and every one or two hours until death; or, as in the case of the control animals, samples were drawn over a time period comparable to the length of life of the experimental group. In some of the control animals it was necessary to repeat the injections of intravenous Nembutal to maintain the animal in a comatose state corresponding in time with that of animals subjected to physiologic hepatectomy. It has been our experience that Nembutal has no appreciable effect on the inhibitor. The blood samples for inhibitor determinations were drawn from the femoral artery into sterile tubes, allowed to clot, then promptly centrifuged at 1,800 r.p.m. for ten minutes. Samples drawn near the time of death from the experimental animals in which clotting was prolonged were refrigerated until clotting occurred. The serum was then decanted into a sterile tube and stored at –25° C. until all samples from any given animal were ready for assay, which was usually the day following the experiment. (Storing of the serum at this temperature for short periods of time results in very little change in the inhibitor value.) The samples were then assayed with the same enzyme preparation and the same substrate. The inhibitor was determined viscosimetrically, employing the method of Hadidian[6] with minor modifications. All determinations were made using the Ostwald type of viscosimeter with a flow time of twenty-five seconds for 4 ml. of distilled water. Experiments were carried out in a constant temperature water bath at 25° C. Reasonable care was exercised to suspend the viscosimeter in the water bath in the same position for all readings. The fluid to be tested was introduced into the larger limb of the viscosimeter until the fluid rose above the bulb in the smaller limb. The "flow time" (time required for the fluid level to fall from a mark above the bulb to a mark just below the bulb) was determined within one-tenth of a second. The volume of liquid used in all determinations was 4 ml. For each set of determinations it was necessary to measure the "final viscosity" (viscosity of the buffer solution) and the "initial viscosity" (viscosity of the buffer solution plus hyaluronic acid). From these determinations the "half viscosity" time was calculated. (The "half viscosity time" is the final viscosity plus one-half the difference between the final and the initial viscosity.) The buffer solution was prepared with the following proportions:

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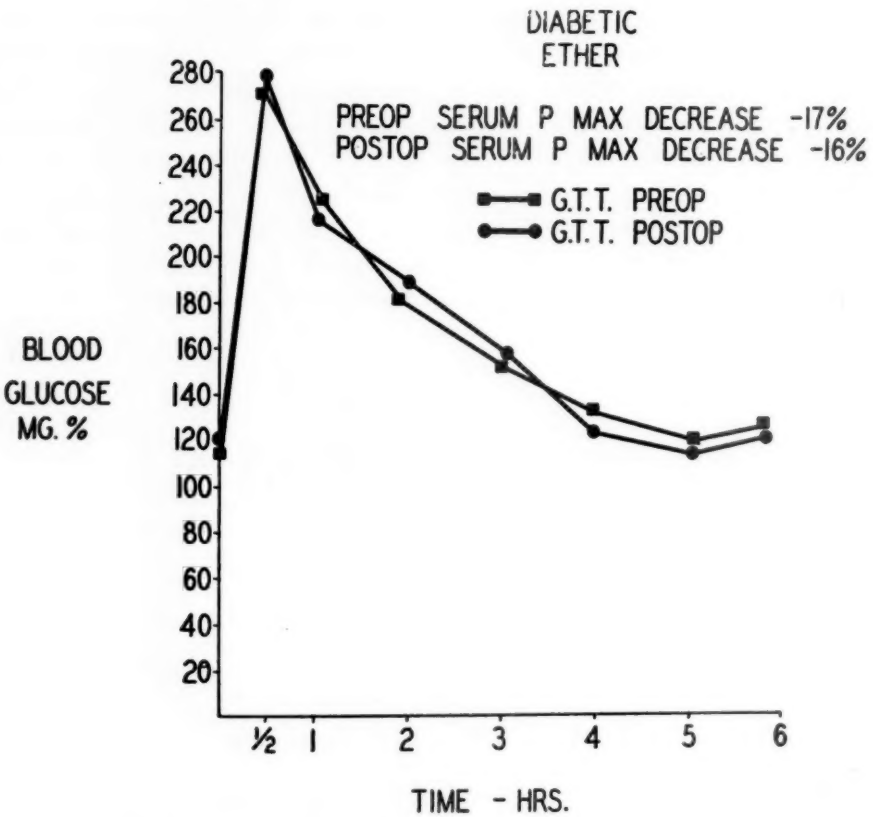

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*Dr. Edward Henderson of Schering Corporation, Bloomfield, N. J., generously supplied us with the hyaluronic acid and hyaluronidase used in these experiments.

by anastomosing the portal vein to the inferior vena cava and completely diverting the venous inflow of portal blood to the liver. The hepatic artery, as well as the entire gastrohepatic ligament, was then ligated, and any anomalous arterial branches noted at the liver hilus. In several of the experimental animals the common bile duct was also ligated, but there was no difference noted in the inhibitor level between these animals and the ones in which the bile duct was spared. Two types of control animals were employed. In one group consisting of two animals, the portal vein was anastomosed to the inferior vena cava in a fashion identical with that used in the experimental group; however, the hepatic artery was not ligated. These animals survived. Another group of six control animals underwent simple abdominal laparotomies and closure of the abdominal incision.

Blood samples for determination of the inhibitor were drawn from all animals preoperatively, at the completion of the operation, and every one or two hours until death; or, as in the case of the control animals, samples were drawn over a time period comparable to the length of life of the experimental group. In some of the control animals it was necessary to repeat the injections of intravenous Nembutal to maintain the animal in a comatose state corresponding in time with that of animals subjected to physiologic hepatectomy. It has been our experience that Nembutal has no appreciable effect on the inhibitor. The blood samples for inhibitor determinations were drawn from the femoral artery into sterile tubes, allowed to clot, then promptly centrifuged at 1,800 r.p.m. for ten minutes. Samples drawn near the time of death from the experimental animals in which clotting was prolonged were refrigerated until clotting occurred. The serum was then decanted into a sterile tube and stored at –25° C. until all samples from any given animal were ready for assay, which was usually the day following the experiment. (Storing of the serum at this temperature for short periods of time results in very little change in the inhibitor value.) The samples were then assayed with the same enzyme preparation and the same substrate. The inhibitor was determined viscosimetrically, employing the method of Hadidian[6] with minor modifications. All determinations were made using the Ostwald type of viscosimeter with a flow time of twenty-five seconds for 4 ml. of distilled water. Experiments were carried out in a constant temperature water bath at 25° C. Reasonable care was exercised to suspend the viscosimeter in the water bath in the same position for all readings. The fluid to be tested was introduced into the larger limb of the viscosimeter until the fluid rose above the bulb in the smaller limb. The "flow time" (time required for the fluid level to fall from a mark above the bulb to a mark just below the bulb) was determined within one-tenth of a second. The volume of liquid used in all determinations was 4 ml. For each set of determinations it was necessary to measure the "final viscosity" (viscosity of the buffer solution) and the "initial viscosity" (viscosity of the buffer solution plus hyaluronic acid). From these determinations the "half viscosity" time was calculated. (The "half viscosity time" is the final viscosity plus one-half the difference between the final and the initial viscosity.) The buffer solution was prepared with the following proportions:

NaCl, 0.5 M.	0.3 ml.
Phosphate buffer, 0.5 M.	0.4 ml.
Borate buffer, 0.2 M.	0.2 ml.
Distilled water	3.1 ml.
Total	4.0 ml.

The buffered hyaluronic acid solution was prepared as follows:

Phosphate buffer pH 7, 0.5 M.	0.4 ml.
NaCl, 0.5 M.	0.2 ml.
Hyaluronic acid sufficient to give 0.8 mg. acid	
Distilled water, necessary amount	
Total volume	2.0 ml.

The enzyme solution was prepared as follows: A standard stock concentrate was made by dissolving 1,000 turbidity reducing units of hyaluronidase in 1 ml. of normal saline solution, 2 ml. of borate buffer, and 7 ml. of distilled water. In high concentration the enzyme solutions remained fairly stable when refrigerated. The "working" enzyme solution was then prepared daily from the stock solution:

Stock enzyme solution	0.5 ml.
Borate buffer, 0.2 M.	2.0 ml.
NaCl, 0.5 M.	1.0 ml.
Distilled water	7.0 ml.

The quantity of enzyme was varied as became necessary to maintain the half time at 180 seconds ± 10 seconds.

Determination of the hyaluronidase activity was then performed in the following manner: The viscosity of 4 ml. of the buffer solution was determined. This represents the final viscosity of the hyaluronic acid solution after complete depolymerization by the enzyme. The initial viscosity was determined next by adding 2 ml. of the previously described hyaluronic acid solution to 2 ml. of the following solution:

NaCl, 0.5 M.	0.1 ml.
Borate buffer, 0.2 M.	0.2 ml.
Distilled water	1.7 ml.
Total	2.0 ml.

This represents the initial viscosity. Then to 1 ml. of the enzyme solution, 1 ml. of distilled water was added. To this mixture, 2 ml. of the acid solution were added and the time noted with a stop watch. The solutions were thoroughly mixed in a test tube, then transferred to the viscosimeter and drawn into the small arm above the bulb. When the level of the fluid fell past the upper mark, the time was recorded (time that had elapsed since the hyaluronic acid and enzyme solutions were mixed) and the clocking of the flow time was begun with another stop watch. This was repeated as often as necessary to obtain a

"half time" for the enzyme, the "half time" being the time necessary for the interaction of the enzyme and hyaluronic acid to reduce the viscosity of the hyaluronic acid solution to that represented by a flow time equivalent to the half viscosity time. Hence the half time is one-half the flow time plus the time elapsed since mixing the enzyme and hyaluronic acid. In instances where the readings of the flow time did not correspond exactly to the previously determined half viscosity time, the half time for the enzyme was determined by interpolation.

To determine serum inhibition, 0.1 ml. of serum was added to 0.9 ml. of distilled water and this mixture added to 1 ml. of the enzyme preparation and allowed to incubate for ten minutes at 25° C. The mixture was then added to 2 ml. of the acid solution and the half time of the enzyme again determined. The inhibition of enzyme activity by the serum we expressed as per cent, employing the formula suggested by Good and Glick[7]: $100\ (R\text{-}R_o)/R$, with (R_o) the half time of the enzyme and (R) the half time of the enzyme after incubation with serum.

Blood samples were also drawn at various intervals during the period of observation for determination of the plasma proteins and hematocrit. Five per cent dextrose in distilled water was administered intravenously throughout the course of the experiment. The rate of flow was changed from time to time in an effort to maintain the hematocrit at a relatively constant value.

The plasma albumin determinations were made with a Klett photoelectric colorimeter according to the method of Kingsley.[8] The hematocrit determinations were made in Sanford-MaGath tubes using liquid heparin as the anticoagulant. The samples were centrifuged for thirty minutes at 2,500 r.p.m.

RESULTS

All the animals subjected to physiologic hepatectomy died at intervals varying from four hours to twenty-one hours following completion of the operation. At autopsy the livers were pale and grossly smaller in size. The portacaval anastomosis was patent in all the animals and the interruption of the main arterial supply to the liver was confirmed by careful inspection. Some of the animals showed a moderate amount of bloodstained ascitic fluid. In ten of the fourteen experimental animals in which plasma albumin determinations were made, there was a significant fall in the plasma albumin shortly before death (Table I). Hematocrit values remained relatively constant for any given experiment. The serum level of the nonspecific hyaluronidase inhibitor fell in all the experimental animals. The decrease in inhibition varied from 2 to 71 per cent, wth an average fall of 29 per cent (Fig. 1). There was no apparent correlation between the percentage fall of the inhibitor and the length of life of the animal.

In five of the control group in which protein determinations were carried out there were only slight variations in the plasma albumin (Table I). It was of interest, however, that the animals demonstrating an increase in the nonspecific inhibitor showed either a corresponding elevation of their plasma albumin or no change. The animals with no alteration or a decrease in the

inhibitor showed a fall in the albumin. This observation tends to substantiate the work of Tobin and associates,[9] who noted a fall in the inhibitor level in protein-depleted rats with a return to normal values following protein repletion. In five of the control animals followed for periods of eight to ten hours, four of the animals showed a slight fall in the inhibitor level varying from 5 per cent to 1 per cent, while one animal showed an elevation of 9 per cent. In the control animals followed for periods of twenty-one to twenty-three hours, two animals demonstrated elevated inhibitor levels of 20 per cent and 16 per cent, and one animal exhibited a decrease of 5 per cent (Fig. 1). The average change for the entire control group was an increase of 12 per cent in inhibitor activity.

TABLE I. ALTERATIONS IN PLASMA PROTEINS IN ANIMALS SUBJECTED TO "PHYSIOLOGIC HEPATECTOMY" AND CONTROLS; CORRESPONDING CHANGE IN THE SERUM INHIBITOR

	PREOPERATIVE VALUES			FINAL VALUES			
ANIMAL	TOTAL PROTEINS	ALBUMIN	GLOBULIN	TOTAL PROTEINS	ALBUMIN	GLOBULIN	PER CENT CHANGE IN INHIBITOR
			Physiologic Hepatectomy				
Ty-4	8.2	4.25	3.95	5.6	3.0	2.6	-16%
Ty-7	5.95	3.52	2.43	3.0	1.84	1.16	-37%
Ty-8	6.70	3.84	2.86	5.1	1.86	3.24	-12%
Ty-9	6.70	5.45	1.25	4.75	3.5	1.25	-13%
Ty-25	5.72	2.74	2.98	3.6	1.87	1.73	-25%
Ty-24	6.0	2.4	3.6	4.95	2.15	2.8	-12%
Ty-27	6.04	3.2	2.84	2.65	1.77	0.88	-31%
Hk-33	6.1	3.3	2.8	3.3	1.6	1.7	-39%
Hk-62	5.6	2.44	3.2	4.3	1.8	2.5	-18%
Hk-64	6.9	3.0	3.9	1.9	1.3	0.6	-54%
			Control Group				
Ty-28	6.7	2.6	4.1	6.1	2.6	3.5	+9%
Ty-34	5.9	3.1	2.8	4.6	3.1	1.5	+20%
Ty-35	5.5	3.1	2.4	5.3	2.6	2.7	-5%
Ty-37	4.1	2.6	1.5	4.8	2.95	1.85	+16%
Hk-65	5.84	3.29	2.55	4.54	2.30	2.24	0%

DISCUSSION

The data obtained from the experiments reported here suggest that the liver represents an important source of the serum nonspecific hyaluronidase inhibitor, as evidenced by a progressive decrease in the titer following physiologic hepatectomy, until death supervenes. This finding is consistent with the aforementioned experiments which have tended to demonstrate that the production of the inhibitor is another of the liver's many functions.

There can be little doubt that an operation of the magnitude performed on these animals has failed to provide adequate physiologic stress. If we accept the concept that the adrenal gland exercises a regulatory role on the serum level of the inhibitor, as recently proposed by Good and associates,[10] it follows that the expected response in these animals with intact adrenal glands would be one of elevated inhibitor levels, unless the source for the inhibitor formation had been compromised. It cannot be inferred from our data that the liver is the sole source of the inhibitor, but it very likely is a major one.

The question immediately arises as to what part death itself may play in the terminal decline of the inhibitor. In this connection we have performed another lethal procedure on dogs, namely, strangulated intestinal obstruction, and have demonstrated a progressive rise in the inhibitor until the animals died.[11]

In light of Glick's recent work[12] pointing out the possible role of a type specific cell in the formation of the inhibitor, it becomes of added interest that the liver is rich in the so-called mast cells. Our findings would apparently lend support to his observations.

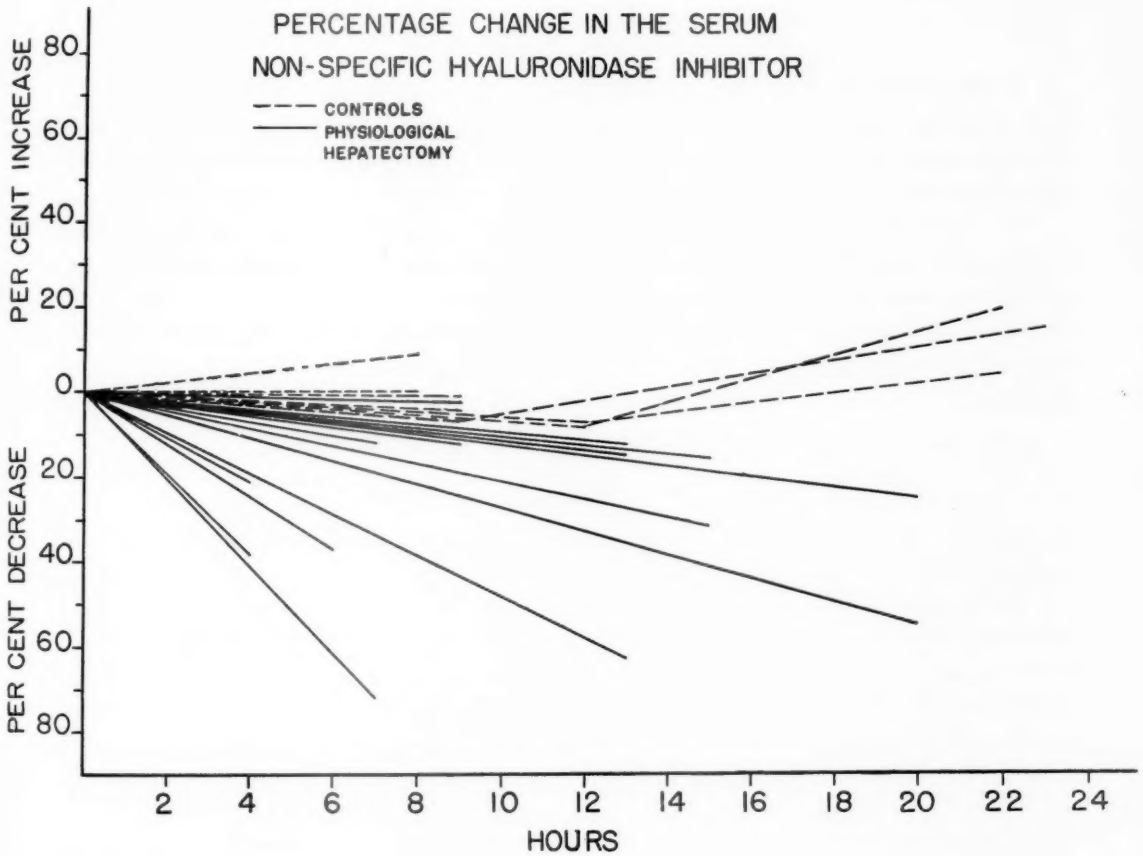

Fig. 1.

Insofar as we have been able to ascertain, very little attention has been focused on changes in the inhibitor during the period immediately following stress. It was of interest that in our control animals there was a slight decrease in the level of the inhibitor during the first twelve hours following tissue damage, suggesting the presence of a "lag" period in the inhibitor response.

Fortuitous circumstances regarding one of our experimental animals provided interesting data. The portacaval anastomosis had been performed on this animal, followed inadvertently by incomplete ligation of the hepatic artery. When it became apparent clinically, after a ten-hour observation period, that the animal was going to survive, we reoperated, ligating the remaining branches

of the hepatic artery. Death followed in approximately eight hours. The inhibitor levels following the initial operation showed a significant decline during the first three hours following the procedure, with a gradual recovery to approximately the preoperative level by the tenth postoperative hour. At this time the second operation was performed with complete ligation of the hepatic arteries, resulting in a progressive fall in the serum inhibitor to a level of 1 per cent as compared to the preoperative level of 17.6 per cent. These findings substantiate our other observations that animals dying from hepatic insufficiency manifest a progressive fall in the inhibitor titer.

SUMMARY

1. Fourteen dogs were subjected to a liver exclusion operation and the level of the nonspecific hyaluronidase inhibitor was determined during the postoperative period. There was a progressive fall in the inhibitor until the time of death.

2. Control animals demonstrated a slight decrease in the inhibitor level during the immediate postoperative period followed by a subsequent rise for periods of twenty-one hours.

3. The data obtained from these experiments suggest that the liver assumes a major role in the production of the serum nonspecific hyaluronidase inhibitor in dogs.

We wish to thank Mrs. Mary Stadler for her technical assistance.

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EVALUATION OF CANCER DIAGNOSIS AT A TEACHING METROPOLITAN GENERAL HOSPITAL, 1944 TO 1950

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A MARKED intensification of interest in the diagnosis of early cancer has been evident during the last few years. Two major influences have been responsible for this attitude: (1) the extensive educational campaign by both lay and professional groups, and (2) the greater awareness of new diagnostic techniques such as the cytologic smear.

It is the purpose of this study to discuss the nature of the cancer cases, both private and service, treated at the Massachusetts Memorial Hospitals, Boston, Mass., during the last seven years. It is intended thereby to establish a working basis for subsequent evaluation of progress in early diagnosis of cancer, particularly by utilization of new laboratory methods.

MATERIAL AND METHODS OF STUDY

The Massachusetts Memorial Hospitals (M.M.H.), a private hospital with 250 beds in the main unit, had an additional 100 beds in a private pavilion from 1947 to 1949. It serves as one of the principal teaching units for the students at Boston University School of Medicine and at least one-half of the cases reviewed herein were private patients of the hospital staff. Furthermore, since the outpatient department from which many of the service cases were referred averages approximately 60,000 visits annually, the statistics of this study would appear to be representative of both the private and the ward services found in a medium-sized, metropolitan general hospital not specializing in cancer therapy. It should be noted that there was little difference in the management of cancer patients of different economic status except perhaps for fewer prolonged hospitalizations for terminal care among the group of service patients.

Eight types of cancer have been included in the present study: colon (including tumors arising as low as the peritoneal reflection), rectum, stomach, breast, lung, cervix uteri (including endocervix), fundus uteri (endometrium), and malignant rectal polyps. Each of 571 cases of pathologically verified cancer treated at M.M.H. from 1944 to 1950 inclusive was analyzed to determine the following facts:

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1. Length of time elapsed between appearance of symptoms and diagnosis.
2. Results of physical examination.
3. Results of special examinations such as roentgenography, bronchoscopy, sigmoidoscopy, cell smear, etc.
4. Method by which final diagnosis was established.
5. Stage of the neoplasm as determined by the pathologist.
6. Operability of the lesion.

In breast cases, only duration of symptoms, stage of disease, and operability were determined. Malignant tumors alone were utilized in this study except in the case of rectal polyps where cases of benign lesions were compiled as well as those of carcinoma.

Cases involving colon, rectum, breast, and stomach have been designated as "controls." This is reasonable since no new, widely applied diagnostic techniques for cancer in these locations were developed during the study years. Consequently, the percentage of early cancers should not have changed greatly in the later years of the study (1947 to 1950) when compared to the earlier years (1944 to 1946), except as cancer education has influenced case-finding.

On the other hand, emphasis on screening chest roentgenograms and exfoliated cell smears from 1947 to 1950 has made early diagnosis of cancer of the lung, cervix uteri, and fundus uteri more nearly a reality. As a consequence, these latter cancers comprise the "test" group. Survey chest films and cytologic smears, if clinically valuable and widely used, should have uncovered more early test group cancers in the latter four years of the study than during the first three years.

CLASSIFICATION OF CASES

Of necessity, certain standards of evaluation of pathological and clinical records were selected, the definitions of which are important if the results are to be interpreted. These are as follows:

1. *Colon.*—

Physical examination: Abnormal findings were defined as palpation of a mass in the abdomen with or without tenderness. Physical findings of acute obstruction were not included in this group.

Instrument examination (sigmoidoscope): Abnormal findings were defined as visualization of a constricted area or a mass in the bowel lumen.

Operable: If an operation was performed without specific mention in the record of palliation alone, the case was considered operable.

Pathologic stage: Since the lymphatic drainage of the colon is so extensive, invasion of lymphatics by malignant cells may be considered to occur early. Therefore, "early" cancer of this organ was defined as that which is restricted to the mucosa or submucosa, and which may locally have invaded lymphatic channels, but not regional lymph nodes. "Moderately advanced" cancer was considered to include those cases in which penetration of the muscularis layer occurred with extension to or within, but not beyond, the serosa; and in which regional lymph nodes were positive for metastases. "Advanced"

cases were those in which the neoplasm went beyond the serosa and invaded neighboring structures by direct extension, or cases in which distant metastases were proved to be present.

2. *Rectum.*—

Rectal examination (digital): Findings were considered abnormal if there was palpation of a mass or constriction with or without fixation of the rectum.

Rectal examination (instrument): Same as colon.

Operable: Same as colon.

Pathologic stage: Same as colon.

3. *Breast.*—

Pathologic stage: "Early" cancer included those cases in which, despite local lymphatic invasion, axillary lymph nodes were negative for metastases. "Moderately advanced" cases were those in which regional lymph nodes were positive for metastases, but not of great size or number. "Advanced" cases included those in which massive, matted, cancerous nodes were present in the axilla, in which there was extensive chest wall involvement, or in which distant metastases were proved to be present.

Operable: Same as colon.

4. *Stomach.*—

Physical examination: Findings were considered abnormal if there was palpation of a mass, or presence of an area of tenderness in the abdomen.

Operable: Same as colon.

Pathologic stage: Here, as in the colon, lymphatics are extensive so that in "early" cancers, regional lymph nodes were negative for metastases. "Moderately advanced" cases had positive regional nodes, and "advanced" cases, direct extension to neighboring structures, or distant metastases.

5. *Lung* (excluding bronchial adenomas).—

Physical examination: Findings were considered abnormal if some findings other than normal were present, when only methods of physical diagnosis (inspection, palpation, percussion, auscultation) were utilized.

Bronchoscopy: Bronchoscopy was considered suggestive of cancer when a mass was visualized, hyperemia of a portion of a major bronchus with abnormal exudation was present (in the absence of infection), or fixation of a major bronchus or the trachea was evident.

Pathologic stage: Same as stomach.

Operable: Same as colon.

6. *Cervix Uteri.*—

Clinical stage (findings on pelvic examination).

0—No abnormalities present (including intraepithelial carcinomas)
I—Lesion confined to cervix
II—Vaginal vault involved
III—Fixation against pelvic wall
IV—Pelvic organs (urinary bladder, rectum, etc.) and/or pelvic bones involved

Pathologic stage: The lymphatic drainage of the cervix is not as extensive as that of the gastrointestinal tract so that invasion of lymphatics may be considered more important here as a criterion of the stage of the cancer. Hence, "early" cases had no local lymphatic invasion, while "moderately advanced" cases did. "Advanced" cases were those in which regional lymph nodes were positive for metastases, there was direct extension to neighboring structures, or there were proved distant metastases. Intraepithelial carcinomas (carcinoma in situ) were those in which malignant changes were restricted to the area distal to the basement membrane of the epithelial lining of the cervix.

7. *Fundus Uteri.*—

Pathologic stage: Same as cervix uteri.

Operable: Same as colon.

The importance of blood vessel invasion could not be assessed in this study since commonly no mention was made of this factor in the records. Lymph nodes have been routinely examined in all tumor specimens from our hospital and the results recorded in all cases.

RESULTS

A period of six months of symptomatology was arbitrarily selected as the limit of "early" clinical cancer. From clinical experience we know that the majority of malignant tumors of this duration which give rise to symptoms will have extensively invaded the organ itself as well as local lymphatics and blood vessels. In the cases studied here, neither the test nor the control groups, during the latter part of the study period, showed any significant difference in duration of symptoms before treatment, as compared to the early period (Table I). This may indicate no essential alteration in the methods of case selection during the study period.

TABLE I. DURATION OF SYMPTOMS REFERABLE TO CANCER

ORIGIN OF CANCER	CASES WITH SYMPTOMS MORE THAN 6 MONTHS IN DURATION		PER CENT OF TOTAL CASES	
	1944 TO 1946	1947 TO 1950	1944 TO 1946	1947 TO 1950
Uteri				
Fundus	19	33	53	58
Cervix	19	39	37	33
Lung	32	68	44	46
Stomach	24	40	30	43
Colon	40	66	45	36
Rectum	19	30	32	37
Breast	43	76	33	32

There was some reduction in "late" colon cancers during the latter part of the study period, with corresponding improvement in the percentage of operable cases. In view of the small number of cases, however, no significance can be attributed to this change (Table II). The physical inaccessibility of colon neoplasms proximal to the sigmoid has required that the tentative diagnosis rest upon a combination of clinical history, physical examination, and

roentgenograms; and the final diagnosis upon exploratory laparotomy (Table III). Occasionally, cell smears of bowel mucus may aid in detection of occult sigmoid carcinoma.[1]

TABLE II. CHANGE IN DISTRIBUTION OF EARLY AND ADVANCED CANCERS OF THE COLON

	40 CASES 1944-1946	66 CASES 1947-1950
Advanced cases	40%	21%
Operable	75%	83%

The present series of cases (Table III) emphasizes the reported failure of barium enemas to reveal colon carcinoma in 10 to 20 per cent of cases.[2]

TABLE III. RELATIVE IMPORTANCE OF METHODS OF DIAGNOSIS OF CANCER OF THE COLON, 106 CASES 1944 TO 1950

Acute obstruction presenting complaint	21%
Rectal bleeding presenting complaint	21%
Physical examination abnormal (except for acute obstruction)	40%
Barium enema suggests malignancy	80%
Final proof of malignancy at operation	94%

Cancer of the rectum has throughout the years offered an excellent opportunity for early diagnosis because of the relatively rapid appearance of symptoms and the ease with which digital and instrumental examination may be done. Therefore, one would expect little further contribution to early recognition of these tumors except from improved lay and professional education. This is illustrated by the fact that preoperative diagnosis was possible in 84 per cent of cases by biopsy alone in the present series of 49 patients. Findings on digital examination were abnormal in 84 per cent of the cases. In those patients who were sigmoidoscoped, abnormalities were found in 100 per cent. Barium enemas suggested malignancy in only 51 per cent of cases.

No remarkable change was noted in the stage of the disease presented by 119 breast cancer patients during the study period, and 91 per cent proved to be operable.

The insidious onset of cancer of the stomach has always made it particularly difficult to make an early diagnosis. It remains primarily a diagnosis by roentgenogram since physical examination is unrevealing in early cases. In the present series of 64 cases, roentgenograms suggested malignancy in 87 per cent, while physical examination revealed abnormalities in only 31 per cent. Gastroscopy has only recently been utilized extensively at this hospital and for the greater part of the study period was not employed as a diagnostic tool. Although cytologic smear techniques have been applied in the diagnosis of suspected gastric cancer,[3] this method was infrequently used in our cases. Therefore, it is impossible to evaluate its worth from this material. In several operable, as well as inoperable, gastric cancers, however, positive smears were obtained. Twenty-two "early" cancers were diagnosed by the usual clinical methods in our series and 80 per cent of the total group were operable. It is

interesting to note that 13 cases of gastric ulcer and 2 cases of pernicious anemia were demonstrated at some time before malignancy was proved. Five of the "early" cancers were from this latter group of 15 cases, a finding which corroborates numerous other reports.[4]

The screening chest roentgenogram and cell smear of bronchial aspirations[5] or sputum[6] offer two valuable methods of making early diagnoses of bronchogenic carcinoma. Neither technique has been used long enough, however, to judge the final value.[7]

Diagnoses of simple infectious processes in the lung are made too often when cancer actually is the underlying cause for the symptoms, abnormal roentgenograms, and clinical signs. In the present series 47 per cent of cases had diagnoses of pneumonia, influenza, etc., made during periods when the malignancy almost surely was present. It is this group of patients in whom cell smears might have been valuable in assisting diagnosis.

In the presence of symptoms roentgenography has been the most readily available method of case-finding. In the present series roentgenographic evidence suggestive of malignancy was present in 80 per cent of patients and misinterpretation of what was later proved to be cancer was present in films of another 13 per cent. Since only 19 per cent of all bronchogenic carcinomas treated between 1944 and 1950 could be classified as "early," chest roentgenographic examination does not appear very dependable as a means of discovering the most favorable cases for operation. This is borne out by the advanced inoperable nature of 6 of the 10 cancers of the lung discovered on routine or survey films in this series. Six of the 10 patients were asymptomatic at the time of the roentgenograms. Four of these 10 cases were discovered by 1950 screening films obtained in programs subsidized by the Commonwealth of Massachusetts.

Physical examination revealed abnormalities in 77 per cent of bronchogenic carcinoma patients while bronchoscopy was suggestive of malignancy in 65 per cent.

A laboratory for interpretation of cell smears was established at this hospital in 1946, but only since 1948 has it been used to any extent. Smears were made of bronchoscopic aspirations and sputum from 45 hospitalized patients in this series, of which one was interpreted as "doubtful," 27 were negative or "inadequate for interpretation," and 17 were "positive." There were no false positives in this last group. Many negative smears can perhaps be explained by technical errors in preparing smears by the bronchoscopist or assistants unfamiliar with the technique of wet fixation. Furthermore, malignancies were often located in such an anatomic position that selection of material for bronchoscopic aspiration was difficult. The advanced nature of most of the lesions probably also contributed to the great number of negative smears. No real evidence for improvement in early diagnosis of lung cancer exists in our series since the resectability rate has remained constant at 36 per cent over the period of observation.

The cell smear is particularly applicable to diagnosis of early uterine cervical cancer. The drawbacks of inexperience with technical details and lack

of well-trained personnel to interpret slides were surmounted sooner for vaginal smears than for respiratory tract material. In the last 2 years it has been possible to employ the test as efficiently and economically in our hospital as in any medical center,[8] but only a small proportion of cases have been examined in this way. Ideally the smear is most valuable in detecting those cases of early carcinoma where a cure is most likely to be effected by modern methods. In the present series 3 in situ cancers were proved in 1949, and 6 in 1950; but in only 3 patients did a positive vaginal smear alert the physician to the possibility of cancer being present. Except for the already mentioned in situ cancers found in 1950, no significant change was evident in percentage of early malignancies discovered in the latter part of the study period when compared to the earlier years.

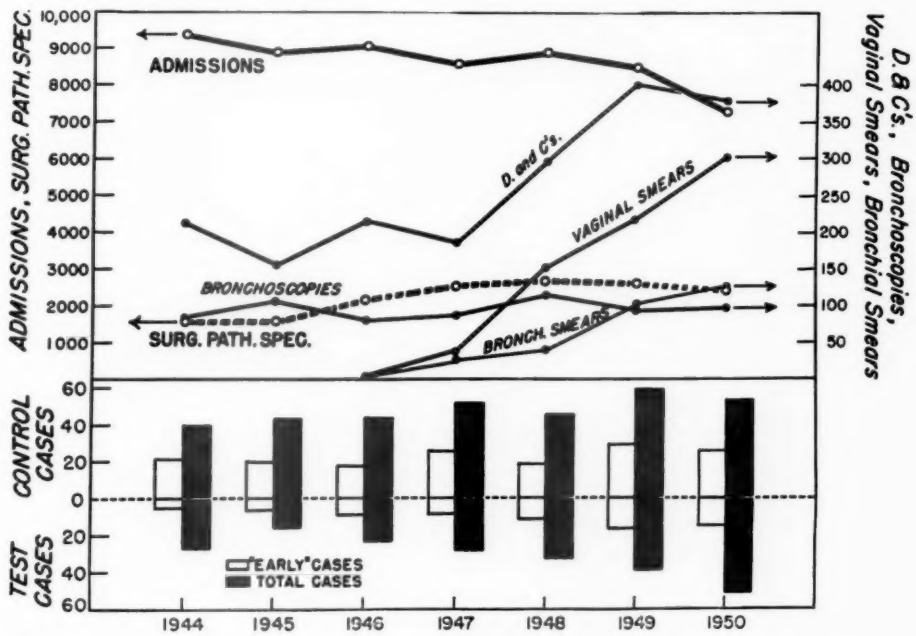

Fig. 1.—Comparison of total hospital admissions, surgical pathologic specimens, dilatations and curettages performed, bronchoscopies performed and cytologic smears taken, with total number of "early" malignancies discovered in test group (lung, cervix uteri, and fundus uteri) and control group (breast, stomach, colon, rectum).

It should be pointed out here that a sharp increase in number of gynecologic patients treated after 1949 took place due to staff changes and the resulting increase in number of diagnostic uterine curettages coincided with this change (Table IV, Fig. 1).

Cancer of the endometrium closely resembles cancer of the cervix in method of diagnosis. The chief features lacking in the former are the absence of positive findings on pelvic examination in most cases and the dependency on uterine curettage for diagnosis. The portion of total cases which were early cancer remained practically unchanged from the early to the later years of the study

TABLE IV. SUMMARY OF STAGE OF DISEASE OF ALL CASES TREATED AT MASSACHUSETTS MEMORIAL HOSPITALS

	1944		1945		1946		1947		1948		1949		1950		1944-1950	
	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL	EARLY CANCER	TOTAL
Controls																
Colon	6	15	8	15	4	10	8	17	4	8	11	22	14	19	55	106
Rectum	4	6	3	6	3	7	3	6	3	3	5	7	6	14	27	49
Stomach	2	5	2	9	4	10	6	10	3	11	5	14	0	5	22	64
Breast	9	14	7	13	7	16	9	19	9	24	9	17	6	16	56	119
Test																
Lung	0	9	2	10	4	13	4	17	3	19	5	17	3	25	21	110
Cervix	2	11	1	5	1	3	3	5	4	7	3	11	7	16	21	58
Fundus	3	7	3	5	4	7	1	6	4	6	8	11	5	10	28	52

period (Fig. 1). Cervical and vaginal smears were insufficiently utilized to judge their value in case-finding. Menstrual bleeding irregularities or postmenopausal bleeding were the diagnostic clues in nearly all cases.

It has been well established that many cancers of the lower gastrointestinal tract start with malignant changes in benign, asymptomatic polyps. The increasing awareness of this fact by physicians is demonstrated in this series, for the number of polyps sent to the pathology laboratory for examination increased from 12 during the first 3 years to 27 during the last 4 years of the study period. There was a corresponding increase in the number of malignant polyps toward the end of the period (11 from 1947 to 1950, 2 from 1944 to 1946), attesting to the value of looking for and removing all polyps found in the rectum or sigmoid colon. Some frank rectal carcinomas may have been prevented from developing by removing these polyps whether they showed recognizable malignant changes or not.

TABLE V. PERCENTAGE OF TOTAL CANCER CASES WHICH WERE "EARLY"

	1944	1945	1946	1947	1948	1949	1950
Control group breast, colon, rectum, stomach	52	46	43	50	41	50	48
Test group lung, uterus	19	30	39	29	34	41	29

The percentage of early "test" cancers discovered from 1947 to 1950 was approximately equal to the percentage diagnosed from 1944 to 1946 in this study (Table V). A steady upward trend in percentage of early "test" cases is evident from 1947 (29 per cent) through 1949 (41 per cent), but in 1950 the percentage fell again to the 1947 level. It is not immediately evident why this regression, if significant, occurred in 1950. Likewise no significant trend was apparent in the control group. The entire period, therefore, shows fairly uniform statistics for the cancers studied here.

DISCUSSION

The data reported here have of necessity been gathered from the files of biopsies and surgical specimens and therefore many advanced and terminal cases are not included. The pathologic specimens, however, include the great proportion of all the most favorable cases reaching the offices of this hospital's staff and the hospital outpatient department. In the majority of cases reviewed here the patients were referred by their family doctors either to the outpatient department or to the private staff, so that this most important factor of selection must be recognized. Since this factor is also often most important in determining the stage reached by the disease at the time of operation, significant improvement in cancer detection in general medical and surgical practice would undoubtedly be reflected in this or similar material.

It would appear from the results of our study that very little practical progress has yet been made in early diagnosis of malignancy. In view of this fact and the small total yearly number of cases, these observations covering 7

years of experience should be pooled and used as a base line for evaluation of future progress. The reasons for this lack of progress rest with both patient and physician—the former because of continued reluctance to have early signs and symptoms properly investigated, and the latter because of failure to utilize all the available diagnostic and screening tools. Because of this, the time lapse between appearance of symptoms and diagnosis did not materially change throughout the study period despite an extensive educational program carried on by organizations devoted to cancer information encouraging patients to seek medical advice when certain "danger signs" were present.

Perhaps the practical limit has been reached in making early cancer diagnoses with the present medical facilities and current diagnostic methods. Nevertheless, it is imperative to evaluate periodically at the local general hospital level the practical results obtained by funds spent by voluntary and governmental agencies for cancer research and teaching. The present study represents one such attempt.

The survey chest film in which considerable reliance has been placed for aiding the early diagnosis of lung pathology has not thus far been shown to be highly productive in case-finding of resectable bronchogenic tumors.[7] This undoubtedly reflects the late radiologic manifestations of this tumor in most instances, owing to its origin in the hilar region of the lungs.

The value of wide application of vaginal smears in clinical practice was shown particularly by Nieburgs and Pund.[8] In 10,000 clinic and hospital cases, 2.5 per cent were shown by this method to have cervical cancer, of whom 42 per cent were asymptomatic and 40 per cent were intraepithelial in nature. Although it is impossible to compare this combined hospital and outpatient experience with that of the present study, it is readily apparent that cervical cancers in our population have been identified with one-tenth that frequency (Table IV, Fig. 1). This is consistent with the infrequency of complete pelvic examination as a routine part of physical examination in most special clinics and on private services of our hospital, and the even less frequent employment of routine vaginal smears. The vaginal and cervical smear is generally accepted at present as offering a most valuable procedure supplementing vaginal examination for the detection of latent cervical cancer.

CONCLUSIONS

1. At a civilian teaching general hospital not specializing in the treatment of malignant neoplasms, the diagnosis of cancer of the colon, rectum, stomach, and breast has remained practically static since 1944, from the point of view of improvement in the stage of the disease when surgically treated.

2. Minimal improvement has taken place in the early diagnosis of cancer of the uterine fundus and cervix in recent years, more because of the wider use of already existing diagnostic tools, such as biopsy and uterine curettage, rather than the use of newer techniques, such as the cell smear. It is recognized that as yet the latter method has not been given an adequate trial by our hospital staff and referring physicians in their office practices.

3. Likewise, since 1944, discovery of early lung cancers has been most disappointing. The growing use of chest survey films should theoretically bring about the discovery of more early bronchogenic cancers than previously, but to date this method has not produced very conclusive results. Examination of sputum and bronchial aspirations for neoplastic cells, although valuable in the diagnosis of some cases, has not yet provided evidence of early, surgically favorable pulmonary cancers in this series. This is probably because its use until now has been restricted only to symptomatic, hospitalized patients with advanced disease.

Acknowledgments.—The authors are indebted to Dr. Rudolph Osgood, pathologist at the Massachusetts Memorial Hospitals, for making available the pathology reports on these patients; and to Dr. Stanley Robbins, director of the Cytology Laboratory of the Mallory Institute of Pathology, for access to records.

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A NEW INTRALUMINAL VEIN STRIPPER*

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IN RECENT years, stripping has become the treatment of choice for varicose veins.

Venous stripping was first described by Keller, in 1905.[1] His method consisted in introducing a wire upward through the saphenous vein and securing the upper end of the vein to the wire, which was withdrawn, invaginating a short segment.

In 1906, Charles H. Mayo[2] introduced the original extraluminal type of vein stripper. This method requires multiple incisions and is technically difficult.

In 1907, Babcock[3] reported his further development of the intraluminal method of stripping, as originally described by Keller.[1] He added an acorn tip to a rigid shaft.

In recent years, Babcock's intraluminal type of stripper has been improved by Linton[4] and by Myers,[5] who have designed flexible shafts. The flexibility allows longer segments of veins to be cannulated and stripped with fewer incisions.

The original Keller stripper has been further modified by Emerson and Muller,[6] Kutz and Hendricks,[7] and by Webb.[8]

The stripper which we are going to describe is intraluminal in type.

CONSTRUCTION

Our instrument consists of five essential parts (Fig. 1): (1) a round metal container, (2) two thirty-six inch flexible cables (The first cable has a threaded obturator on each end. The second cable has a threaded obturator on one end and a leaded swivel between the threaded obturator and cable on the other end), (3) probes, (4) stripping heads, (5) a detachable handle.

1. Our stripping outfit is held in a specially designed container which holds the cables, stripping heads, and probes. This results in one compact unit made round in an effort to preserve the original construction of the cables and to prevent kinking during storage. On the bottom of the steel box, five studs are arranged in a circle on which the two probes and two stripping heads are fastened. The longest probe is left attached to the stripping cable during storage because its length would make closure of the container impossible, if placed on a stud. The two cables are coiled around the sides of the box and the detachable handle rests on the bottom. The top and the bottom of the box have been suitably perforated so that the entire container, with its contents, can be

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*Manufactured by George P. Pilling & Son Co., Philadelphia, Pa.

put into the boiler or autoclave for sterilization. After sterilization, the whole unit is placed on the operating table and the surgeon works directly from the metal container while stripping.

2. The shafts we are using are made of woven, stainless steel airplane control cable. This type of cable is strong and moderately stiff, but it has enough flexibility to follow a tortuous vein. These are approximately 36 inches in length and will easily reach from the internal malleolus to the inguinal region. A small threaded boss is silver-soldered to each end of each stripping cable to receive the various probes and heads. One cable is called the countertraction cable and is varied somewhat in that one end is fitted with a fishline swivel, between the small threaded boss and the main portion of the cable.

3. There are three probes. One is a round ball, 5/16 inch in diameter. The second probe is somewhat cone-shaped and is 1½ inches long and 3/16 inch in diameter at its base. The third probe is also cone-shaped and is ¾ inch long and 5/32 inch in diameter at its base.

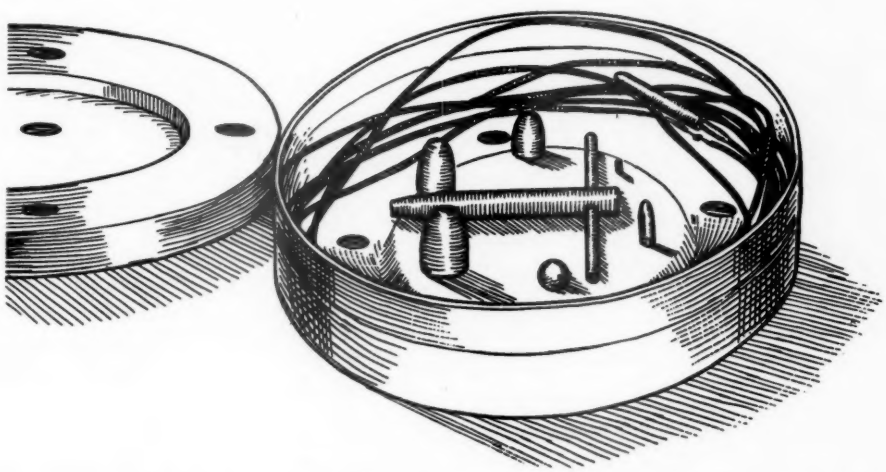

Fig. 1.—A circular steel box containing the flexible stripping wires; the probes and stripping head are threaded on studs in the bottom of the box; the detachable handle rests on the bottom; the top and bottom of the box are perforated to permit boiling or autoclaving for sterilization.

4. The three stripping heads are 3/8, 7/16, and ½ inch in diameter. All heads and probes are threaded 1/8 by 40 threads per inch, the heads being threaded straight through the center, while the probes are threaded in the bottom only. We feel that the best stripping cable is 1/16 inch in diameter.

5. All parts of the apparatus should be stainless steel or other suitable noncorrosive metals. This includes the simple detachable handle that can be threaded on either end of our traction cable.

USE

The entire unit, including the round metal box, is sterilized and placed on the surgeon's instrument table.

The lower abdomen and legs are prepared as in any vein stripping procedure. A transverse incision is made on one side, over the saphenous bulb in

the subinguinal region (Fig. 2). The tributaries of the saphenous vein are clamped and ligated, the saphenous vein is doubly clamped and incised, and the proximal end is doubly ligated. The clamp is then left on the distal end, as that is the portion to be stripped. A longitudinal incision is then made over the lower end of the internal saphenous vein, anterior to the internal malleolus at the ankle (Fig. 2). The vein is identified, doubly clamped and incised, and the distal end is ligated.

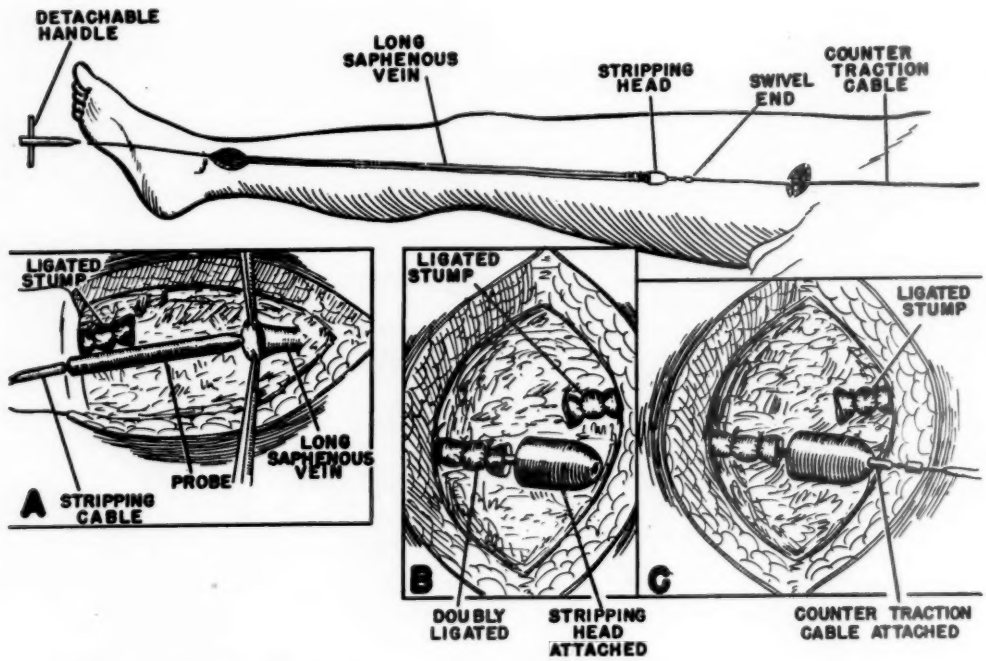

Fig. 2.—The top picture shows the entire extremity, with the detachable handle on the lower end of the main stripping cable. The stripping head has the countertraction cable attached to it. The stripping procedure is revealed as traction is made downward, showing the vein plicating itself behind the stripping head. The countertraction cable is useful in maintaining a straight pull and sawing action.

A.—A stripping cable with a probe attached being inserted into the lower end of the long saphenous vein. The vein is held open with mosquito forceps.

B.—The probe has presented itself at the upper end of the saphenous vein in the thigh and has been replaced by the desired stripping head. The vein is doubly ligated behind the stripping head to prevent inversion.

C.—The upper end of the saphenous vein, with the stripping head attached, and the countertraction cable, with its swivel end screwed into the end of the stripping head.

The stripping cable, with a probe the proper size for the vein, is passed upward from the lower end of the saphenous vein at the ankle (Fig. 2*A*). After removal of the hemostat, the probe emerges at the thigh incision (Fig. 2*B*). The probe is then removed and replaced by a stripping head of the proper size, which is determined by the size of the vein (Fig. 2*B*). The vein which is to be removed is ligated in two or more places behind the stripping head. This prevents invagination of the vessel with rupture and partial removal (Fig. 2*B*).

The swivel end of the second, or countertraction cable, is now screwed into the rounded end of the stripping head (Fig 2*C*). The swivel is advantageous in that it permits the insertion of the countertraction shaft without turning the

entire length of the cable. This second cable is controlled by the assistant. It allows for complete control of the stripping head, thus keeping the base at right angles to the vein. It also supplies a means for a seesaw motion, if a large venous tributary is reached and causes resistance. However, should the vein break as it is being removed from above downward, the traction cable can be pulled back through the upper incision. The stripping head can be detached and reapplied to the threaded obturator at the ankle. Then the countertraction cable can again be placed into the stripping head and the vein stripped from below upward.

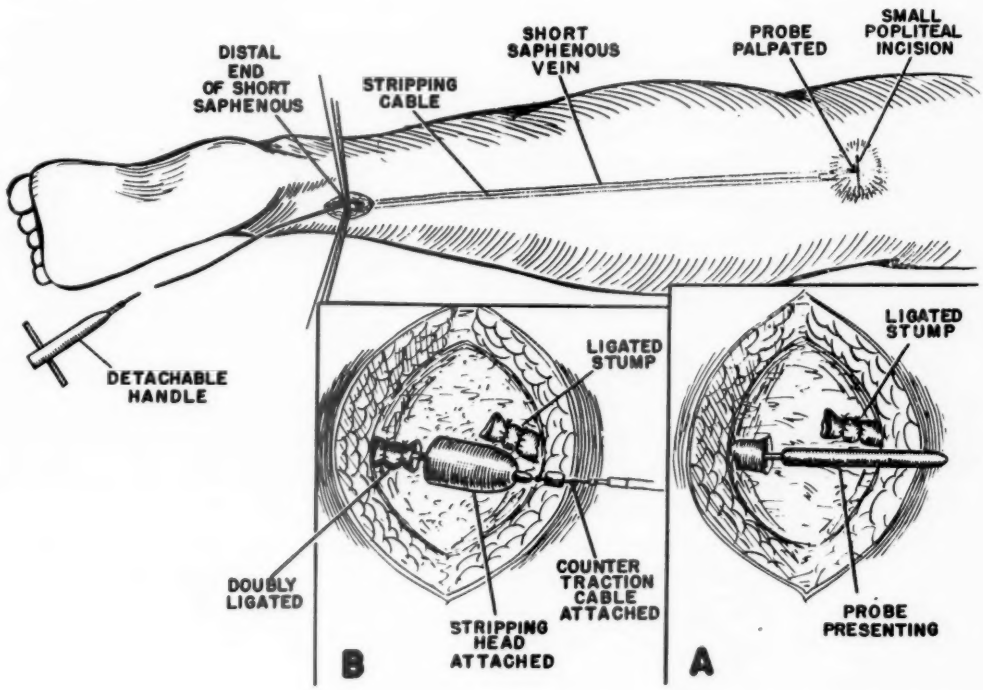

Fig. 3.—The top picture shows the vein being prepared for stripping from above downward by pull on the detachable handle.

A.—The probe is palpated, a small transverse incision is made, the vein is transected, and the proximal end is ligated

B.—The probe is replaced with a stripping head and the countertraction cable. The vein is doubly ligated behind the stripping head.

The detachable handle is always applied to the stripping cable and controlled by the surgeon (Fig. 2). This offers one main advantage in overcoming the tendency of the operator or the assistant to twist the cable to make his own handle, thus eventually kinking the wire. As the stripping head is pulled downward through the leg, the vein begins to pile up behind it. The assistant makes a countertraction on the second flexible cable from above, keeping the stripping head perfectly aligned, so that it does not twist and cut the vein to be stripped (Fig. 2).

We believe that it is best to remove the vein with only two incisions, as just described. The passage of the stripper from the sapheno-femoral junction to the internal malleolus is possible in only a small percentage of cases. It may

pass into a branch, or impinge upon a remnant of a valve, thus requiring extra incisions to correct the difficulty. We have found it more efficient to pass the flexible shaft from the internal malleolus upward, as the convergent branches of the vein and the valve cups allow it to pass more easily. Since our instrument is threaded from either end, it is possible to strip from either direction, but we prefer to do it from above downward. The opposite direction may cause the vein to invert upon itself and a large branch may cause rupture of the main vein. However, should this occur, the process can be immediately reversed, with the stripping head placed on the opposite end of the shaft. Then the remaining portion of the vein can be stripped from the opposite direction.

After removal of the long saphenous vein, the wounds are closed in the manner most desirable to the surgeon. Then the long saphenous vein on the opposing leg is stripped, if it is incompetent.

The short saphenous veins are more easily stripped if the patient is placed face downward on the operating table. The legs are again prepared and draped. A small longitudinal incision is made one fingerbreadth anterior and lateral to the Achilles tendon, at the level of the external malleolus (Fig. 3). The short saphenous vein is identified, doubly clamped, incised, and the distal end is ligated (Fig. 3). The proximal end of the vein is held open with mosquito forceps and the stripping cable, with the proper-sized probe, is gently pushed up through the vein to the popliteal fossa (Fig. 3). The probe is easily palpated and identified through a very small transverse incision (Fig. 3). The proximal end of the vessel is ligated after transection of the vein between clamps. The distal hemostat is then removed and the probe presented into the wound by gentle upward pressure on the stripping cable, at the ankle (Fig. 3*A*).

The probe is then removed and replaced by an appropriate sized stripping head. The vein is ligated in several areas behind the head to prevent invagination (Fig. 3*B*). The swivel end of the second, or countertraction cable, is now screwed into the rounded end of the stripping head (Fig. 3*B*). The detachable handle is applied to the end of the shaft, presenting itself at the ankle incision (Fig. 3). With the assistant applying tension, the surgeon then strips the vein from above downward. If the vein breaks during this process, the assistant pulls the stripping head back through the popliteal incision. Without recannulating the vein, he applies the stripper and countertraction mechanism at the ankle, and completes the procedure from the opposite direction.

The wounds are closed and the opposite vein can be removed, if so indicated. After removal of the veins, we prefer to apply pressure to the operated areas with elastic bandages over sterile dressings.

CONCLUSION

We have used this new type of intraluminal stripper for a portion of the past year and have done venous strippings on some fifty extremities with very satisfactory results.

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LUMBAR INTERVERTEBRAL DISC SURGERY

Description of a New Instrument, The Vertebra Spreader

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IN THE early days of intervertebral disc surgery, the lesion was approached by total removal of one or more laminae, the dura mater opened, the cauda equina retracted, and the herniated fragment of the disc removed through an incision in the anterior dura.[1-3]

It soon became apparent that such a wide opening in the spinal canal was unnecessary for the removal of such a small, well-localized, and usually unilateral lesion. The exposure by a hemilaminectomy was next used.[4, 5] The dura mater still had to be opened to remove the thick, viscid Lipiodol used to demonstrate the lesion roentgenologically.

Following the early articles of Love[6] and others, the bony opening into the spinal canal became smaller—the interlaminar approach. After removing the ligamentum flavum, a small notch was made in the edge of one lamina, or if the interlaminal space was sufficiently wide, surgeons boasted of "removing the disc" without removing any bone!! This "keyhole" opening was considered adequate for the removal of the herniated fragment of the ruptured disc compressing the nerve root. This opening is used by many neurosurgeons today, particularly since the advent of the less viscid and readily aspirated Pantopaque oil used for myelography, which obviates the necessity of opening the dura mater for its removal. In recent years, more and more spinal fusion operations are being done in conjunction with removal of the intervertebral disc. The neurosurgeon is requested by his orthopedic colleagues to remove as little of the lamina as possible for the intraspinal procedure, to assure a successful posterior type of spinal fusion.

It has been the experience of every surgeon doing intervertebral disc surgery for the patient to continue to complain of leg pain or to develop a recurrence of their symptoms soon after the operation. The causes of these surgical failures have been recognized by the writer for many years,[7, 8] and others have more recently described them.[9, 10] The most frequently encountered are: unstable vertebral joint due to loss of the nucleus pulposus; the existence of other disc fragments herniated beyond the visual limits of the operative exposure; the existence of arthritic spurs encroaching on the intervertebral foramen; and narrowing of the foramen due to encroachment of the articular facet following collapse of the disc. It is apparent that an adequate investigation and removal of these abnormalities cannot be made through a keyhole opening in the bone of the spinal canal.

In 1943, because of frequent recurrence of symptoms of patients operated upon for ruptured intervertebral disc, the writer began experimenting with a

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different type of operation.[7] The purpose of the procedure was to immobilize the loose vertebral joint by effecting a bony fusion of the vertebral bodies. This was first attempted by removing a part of the intervertebral disc through a hemilaminectomy, and replacing it with a large bone plug. The operation has been gradually improved until at the present time it has reached the stage of near perfection. The operation as done today consists of a subtotal removal of the lumbar disc, including the cortical surfaces of the adjacent vertebral bodies, and the driving of three or more full-thickness bone grafts, removed from the iliac crest, into the intervertebral space. This is done through a partial bilateral laminectomy.

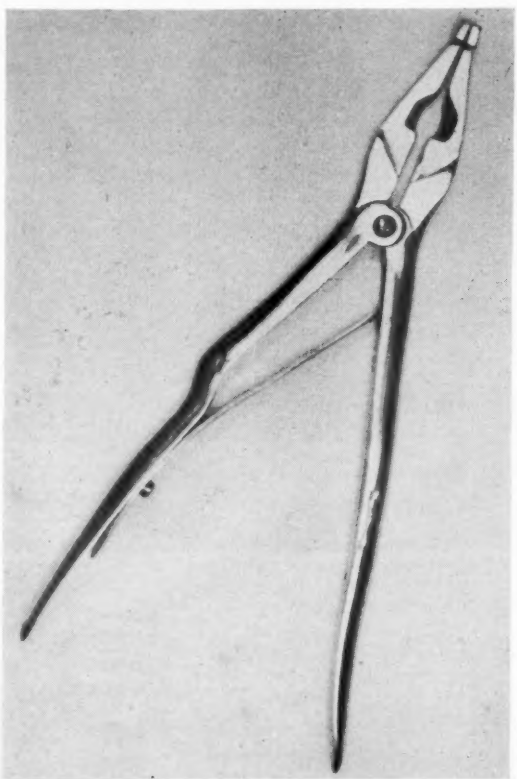


Fig. 1.—The vertebra spreader (closed). Note broad tips for engaging the retractor on lamina (for manual spreading).

This operation of fusing the bodies of the vertebrae has been considered for many years as the most logical and physiologic method of spine fixation. It has been described and attempted by several authors.[11-13] The surgical approach to the vertebral bodies, however, was made through the abdomen. Because of technical difficulties and high morbidity rates, these operations seldom have been used. The vertebral body fusion through the spinal canal has always been considered by orthopedic surgeons[14] as too hazardous ever to be practical or feasible.

The writer has performed over 265 vertebral body fusions since 1943 by the posterior approach.[15] For the purpose of obtaining a greater exposure

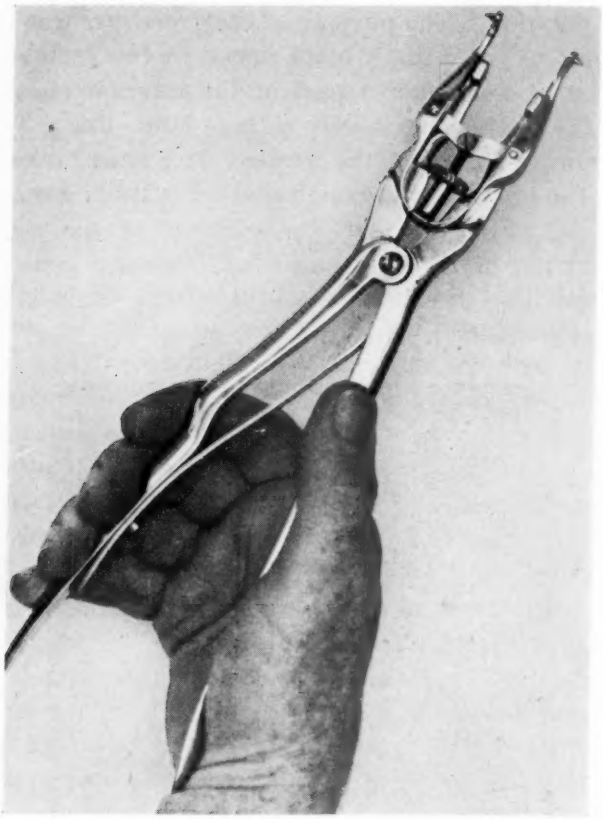
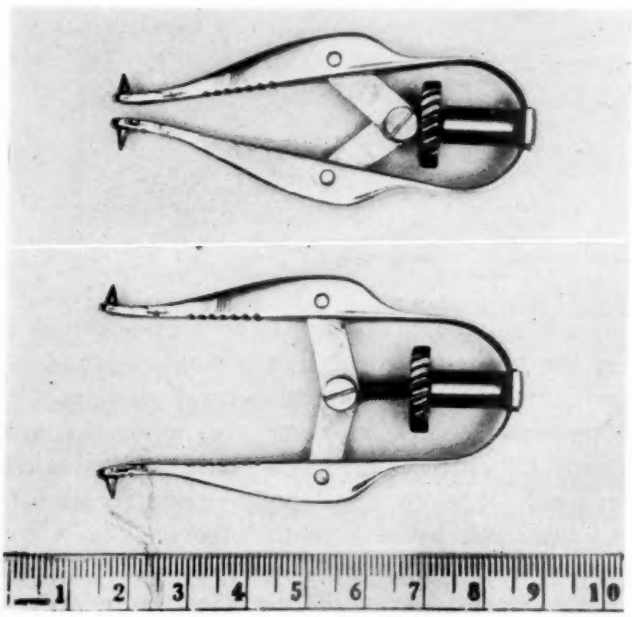


Fig. 2.—The vertebra spreader and retractor as used together.

A.



B.

Fig. 3.—The vertebra retractor *A*, closed, *B*, open.

of the anterior wall of the spinal canal and the intervertebral disc, several instruments have been devised for this operation to separate the lamina and widen the intervertebral space. As a culmination of these experiments over a period of years, a self-retaining vertebra retractor finally has been developed which is small, practical, and easy to use. This instrument has greatly simplified what has been called a "tedious and difficult operation."[16]

Fig. 4.—The interlaminar opening into the spinal canal and intervertebrae space with the vertebra retractor in place.

The instrument* consists of two separate parts, the spreader and the retractor. The spreader (Fig. 1) looks like a long-handled bone rongeur but, instead of cutting blades, there are two short jaws which spread like open scissors when the handles are closed together (Fig. 2). The end of each jaw is equipped with a small rough plate which can be placed between the spinous processes or lamina for manual spreading or engaged in the retractor for the purpose of separating it.

The retractor is spring steel, horseshoe-shaped, and approximately 3½ by 1½ cm. in size. The open ends of the "horseshoe" are in contact with each other in the closed position (Fig. 3). They are equipped with single sharp points which are engaged in the cancellous bone of the vertebral spines or laminae to prevent slipping. The "legs" of the retractor are separated to the desired width with the spreader (Fig. 2), and are fixed or retained in this open position by twirling a small knurled nut (Fig. 3*b*). The spreader is then removed leaving the retractor in place. Being of small size, it remains to one

*Manufactured by Codman & Shurtleff, Inc., Boston, Mass.

side of the wound, out of the way, while the operator works on the other side of the midline. In hemilaminectomies, or unilateral operations in which the lumbodorsal fascia and muscles are removed from the spinous processes and lamina only on one side, the retractor is placed between the tips of the spinous process (after detaching the interspinous ligament). In bilateral operations (Fig. 4), used for the vertebral body fusion, the retractor is inserted between the laminae, first on one side of the midline, then the other. The bone grafts are inserted on both sides of the dural sac.

For the neurosurgeon who desires to continue with the keyhole operation for ruptured intervertebral disc, the use of this instrument will prevent many disappointing failures, as described by Greenwood and associates,[9] by permitting a much wider interlaminar exposure without removal of too much bone. This will be appreciated by the orthopedic surgeon who contemplates a posterior type of spinal fusion. For those who wish to do the anterior (vertebral body) fusion, which in the author's experience has given results far superior to any operative procedure yet reported for ruptured intervertebral disc, the instrument is indispensable. This instrument when used with the self-retaining dura retractor[16] has made the surgical procedure for lesions anterior to the spinal dura mater safe and relatively simple, rather than difficult and hazardous. It has likewise made an operation for bony fusion of the vertebral bodies almost as easy and not much more time consuming, in the hands of an experienced neurosurgeon, as a "simple" disc removal.

The orthopedic surgeon will find the vertebra retractor especially useful for posterior spinal fusions. In performing the Hibb's spinal fusion, most orthopedic surgeons remove a large section of the superior articular facet. It is necessary to open up this joint space in order to remove the cartilage, gouge up the cortical bone, and pack it with fine or large bone grafts to assure a solid facet fusion. With the vertebra retractor the articular facets can be spread and held so wide apart that the cartilage removal, chiseling, and packing process can be done without removing part of the facet. This assures a heavier bony support at the facet, and is conducive to a more rapid and stronger fusion.

In the fusion operation so popular today, of inserting an "H" or "clothespin" graft between the spinous processes, this instrument is especially helpful. By placing the spreader between the laminae, a wide separation of the spinous processes can be obtained and held until the graft is inserted.

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Case Reports

SHORT-TERM SURVIVAL FOLLOWING MASSIVE SMALL BOWEL RESECTION

CASE REPORT

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THERE have been, in recent years, an increasing number of reports of long-term survival after extensive small bowel resection. With the ancillary aids of modern anesthesia, fluid therapy, and antibiotics, more people survive the operative period. It is of interest that Evans and Breniger,[6] in 1907, and Flint,[7] in 1912, by experimental investigations in extensively resected dogs, demonstrated most of the important consequences known today.

A brief summary of the important factors follows: (1) The most common cause for the necessity of extensive resection is massive volvulus or mesenteric vascular occlusion. (2) There is great individual variation in ability to maintain adequate digestion and assimilation. In general, most patients will tolerate well 50 per cent resection of the small bowel. (3) In general, carbohydrates are utilized most efficiently followed by proteins and fats, in that order.

We believe the following case is worth adding to the literature because at least short-term survival was possible even though, in addition to extensive enterectomy, the patient had previously had a high subtotal gastrectomy for gastric carcinoma. This case is very similar to one, published by Weckesser and associates,[11] of a patient who had 60 to 75 cm. of small bowel remaining after a resection for massive volvulus which occurred two years following subtotal gastrectomy for benign ulcer. Their patient died of inanition nine months following operation.

CASE REPORT

G. H. (U.H.N. 89555), a 55-year-old Negro man, was first admitted to the Pennsylvania Hospital for treatment of carcinoma of the stomach. A radical subtotal gastrectomy of the Hofmeister type was performed on March 13, 1950. There was no evidence of distant metastases at that time. A two-tube jejunostomy, as described by Allen and Donaldson,[1] was also performed to allow simultaneous gastric decompression and jejunal feedings in the postoperative period. The patient withstood the procedure well, and the postoperative period was without complication. He was discharged on the eleventh postoperative day

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weighing about 59 kilograms. He was placed on a modified ulcer diet. The pathologist reported "adenocarcinoma of the stomach, grade III-C, with 22 adjacent lymph nodes negative for metastatic tumor."

On June 23, 1950, three and one-half months after operation, while eating supper, the patient was seized by crampy abdominal pain associated with nausea and vomiting of bile-containing material. When seen six hours later, his abdomen was slightly distended and rigid. There was little tenderness. Peristalsis was hyperactive. The white cell count was 22,000, hemoglobin 13.5 Gm. A roentgenogram of the abdomen revealed several dilated loops of small bowel suggestive of intestinal obstruction. Abdominal distention rapidly increased and the patient went into peripheral circulatory collapse. He was prepared for operation as rapidly as possible with intravenous fluids, blood, and intestinal suction.

At operation, the peritoneal cavity was found to contain approximately 1,000 c.c. of foul, thin, grayish black fluid. There was a volvulus of almost the entire length of the small bowel. The bowel was obviously nonviable from a point 10 cm. below the gastrojejunostomy to within 7½ cm. of the cecum. The entire intervening segment was rapidly removed and an end-to-end anastamosis made. There was no evidence of recurrent carcinoma nor was any likely cause for the volvulus found. The abdomen was closed in layers about a pelvic drain. At the time of closure it was estimated that about 17½ cm. of small bowel remained between the stomach and cecum. The resected bowel measured 720 cm. in length. The patient's immediate postoperative course was surprisingly benign. On the fourth postoperative day, intestinal contents appeared around the drain, however, indicating a leak at the anastomosis. Water taken by mouth would emerge from the wound in a matter of seconds. Because of this fistula, oral feedings were withheld and the patient was sustained parenterally for a prolonged period. The fistula gradually closed and intravenous fluids were stopped July 27, 1950, one month postoperatively. During that month he received, in addition to his daily fluid requirements, multiple transfusions and intravenous protein hydrolysate, some of which contained 5 per cent alcohol.

During this period, the total serum protein dropped from 6.2 Gm. per cent to a low of 4.7 Gm. per cent. The hemoglobin was maintained at about 11 Gm. per cent. The blood calcium never dropped below 8.9 mg. per cent. His weight dropped from 59 kilograms to 50 kilograms. On August 4, a barium meal revealed a segment of small bowel measuring, on the film, 23 cm. from the remnant of stomach to the cecum. In one hour, the head of the meal was seen in the descending colon. After two hours, there still remained some barium in the stomach remnant (Fig. 1).

The patient was placed on a carefully weighed diet, high in protein and carbohydrate, which he took well. His meals were broken up into eight or ten small feedings daily. Liquids were taken between feedings. In addition, bismuth and paregoric were given. He passed from five to ten stools daily, all of which were semisolid or liquid and contained undigested food. After two weeks, he was given polyoxyethylene sorbitan monoleate, a wetting agent, in the hope of increasing absorption from the bowel wall.[10] No change in the stools or body weight was manifest. Although the serum protein and body weight did not rise appreciably on this regimen, the patient regained strength and was discharged two months after operation, on Aug. 29, 1950, weighing 52 kilograms.

Three weeks later he returned in a markedly dehydrated condition weighing only 43.6 kilograms. He had not eaten a meal for two weeks due to extremely poor home conditions. With hydration, his weight jumped from 43.6 to 49 kilograms in one week. His blood chemistries were not remarkable except for the serum protein which remained at about 5 Gm. per cent. He was found to have a moderate hypochromic, microcytic anemia. Bone marrow studies were normal and the stools were negative for occult blood.

He was tried on diets which varied in caloric content and in the proportion of protein, carbohydrate, and fat without clinical effect. He faithfully ate all food offered. In spite

of all measures, he passed three to five liquid stools daily and his weight steadily dropped to 44.1 kilograms. He seemed to deteriorate at ever increasing speed.

On Nov. 2, 1950, a roentgenogram of the chest revealed activation of an old tuberculosis and a smear of the sputum revealed acid-fast bacilli. The patient, heretofore cheerful and cooperative, gave up all hope and signed himself out against advice, Nov. 9, 1950. He died at home, Nov. 29, 1950, five months after his second operation. Permission for autopsy could not be obtained.

Fig. 1.—Roentgenogram taken shortly after the ingestion of a barium meal. The patient's entire small bowel is outlined as it connects the stomach remnant, seen in the upper right-hand corner of the film, to the cecum in the lower left-hand corner. This segment measures 23 cm. on the film. The short transverse pattern of barium overlying the fourth lumbar vertebra is thought to represent reflux of barium into the defunctionalized duodenum proximal to the gastrojejunostomy.

DISCUSSION

Estimates of the normal length of the small bowel in the human range from 21 feet, 6 inches, to 26 feet (645 to 780 cm.).[5, 8] Experiments on dogs have shown that removal of one-half of the small bowel is usually tolerated well.[7] Dogs with seventy per cent removal required meticulous postoperative care for survival. Cattell[2] reported the removal of 86 per cent of the small bowel of a 70-year-old patient who suffered no disturbance afterward. Chodoff,[3] in 1950, reported the removal of all but 35 cm. of jejunum in a patient with mesenteric vascular occlusion who survived with only minor nutritional disturbances, only to die a cardiac death five months later. Weckesser[11] reported the case of the only other patient we could find in American literature who had had a previous gastrectomy. He removed all but 60 cm. of jejunum for volvulus two years after the gastrectomy. His patient pursued a gradual

downhill course and died of inanition in nine months. The reported patient survived for five months following removal of the major portion of his stomach and all but an estimated 23 cm. of his small bowel.

It has been suggested[7] that, following a massive resection of the small bowel, the remaining portion will hypertrophy, principally through an increase in diameter. In our case, roentgenograms two months postoperatively failed to reveal this effect. Furthermore, there appeared to be little difference in the character or frequency of the patient's stools between the second and fifth months postoperatively, indicating failure to adapt to the lessened absorptive surface.

The use of an enteric wetting agent was described by Jones[10] as aiding intestinal absorption where difficulties were encountered following gastrectomy. Weckesser employed it in his case without benefit. Results in our case were similarly disappointing.

Previous writers,[3, 9, 11, 12] after trying various diets, have found that one containing a high proportion of carbohydrate, medium protein, and low fat was best utilized by their patients. In our patient, little difference was noted in the character or frequency of stools or in the body weight as various diets were tried.

Hypocalcemia and tetany have been described[4, 9, 12] as a complication of massive intestinal resection. Holman[9] attributed the hypocalcemia to the fact that calcium is lost in the stools having been combined as soap with the fatty acids which are lost in excess. There was no tetany in the case we reported. The lowest of several serum calcium determinations was 8.9 mg. per cent.

The survival in our case was unquestionably shortened by pulmonary tuberculosis and poor home conditions. There was no evidence of recurrence of the carcinoma at the second operation, but this, too, may have played a role in the patient's downhill course. It is interesting to conjecture what might have been his fate had these factors been absent.

SUMMARY

A case is reported of resection of all except about 23 cm. of small bowel for volvulus in a patient who had three months previously undergone subtotal gastrectomy for carcinoma. The patient died five months following the second operation after a gradual downhill course. The pertinent literature is reviewed.

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DIVERTICULITIS OF THE CECUM

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IN THE differential diagnosis of lesions causing signs of peritoneal irritation in the right lower abdominal quadrant, with or without a mass, cecal diverticulitis must be considered. This condition is less uncommon than is ordinarily supposed. Byrne and associates, in November, 1950, published five cases, bringing the total number of reported cases up to 126. The true incidence is probably higher. Apart from cases which have not reached the literature, others for which laparotomy was performed for acute appendicitis may have been subjected to routine appendectomy without the surgeon's looking further for a more adequate explanation of the symptomatology than the not significantly inflamed appendix. In other instances an abscess, supposedly appendical in origin, may have been encountered and drained. A better idea of the incidence may be obtained from Ochsner and Bargen's figures of a 2 per cent occurrence of diverticula of the right colon in 151 cases of uncomplicated diverticulosis. Fourteen per cent of these diverticula became inflamed, and 15 per cent of those inflamed required surgery. Epstein, quoting Sprigg and Marker, gave a somewhat higher incidence of right-sided diverticula. In 1,000 routine x-ray studies of the colon, 100 diverticula were demonstrated. Of these, twenty-two occurred in the right colon, of which seven were in the cecum. Applying the 14 per cent inflammation rate given by Ochsner and Bargen, which is also that given by Anderson in his report from the Mayo Clinic, it is seen that diverticulitis of the cecum is not rare.

Diverticula in the cecum, as elsewhere in the intestinal tract, have been classified into two types, congenital and acquired. The congenital diverticulum is described as an outpouching of all layers of the cecal wall, usually arising near the ileocecal valve and resembling an extra appendix. This type is rare. Greensfelder and Hiller suggest that it may represent the retention in some residual form of the appendix which appears early in embryonic life but normally disappears before the true appendix develops. The acquired type in the left colon is a "false" diverticulum consisting of a hernial protrusion of the mucosa and submucosa. In the cecum, designation as congenital or acquired on the basis of the presence or absence of a muscularis is unsound, as various etiological mechanisms operate which differ from those causing left-sided diverticula. In some cases these may produce diverticula including all layers, while in other instances the muscularis may be absent. Moreover, in long-standing cases the muscularis may become attenuated and replaced in large part or entirely by fibrous tissue, which makes even less satisfactory this criterion for classification into false and true.

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For several reasons the cecal diverticulum appears to be a different entity than that found elsewhere in the colon. First, it is usually solitary. Second, as against a definite preponderance among male patients in sigmoid diverticula, the sex distribution is about even in the cecal variety. Third, the lack of correspondence of the diverticula with the location of epiploic appendages and the absence of the localized pulsion force of solid stool make these factors less applicable in the cecum.

Various etiological mechanisms have been suggested. Bunts reports a case of diverticulum occurring at the site of amputation of an appendix, and attributes its development to relaxation of the purse-string suture with eversion of the inverted portion of the gut. Horsley states that the purse-string method of appendectomy is an important factor in the etiology of diverticula, and quotes Bunts as ascribing the process to the destruction of the circular fibers around the base of the appendix by the purse-string suture. This, obviously, explains only a small percentage of cecal diverticula as many, if not most, do not develop at the site of an appendix stump. Darling suggests a traction mechanism. The traction may be caused by the contraction of scar tissue, from nonspecific inflammation or ulcer of the cecum. Or, it can be associated with tuberculous mesenteric glands. Greensfelder and Hiller, on the basis of experimental studies and necropsy findings, suggest one or a combination of several of the following mechanisms for the acquired types:

1. Eversion of the cecum between two constricting adhesive bands
2. Traction of a narrow adhesion
3. Eversion of an appendical stump site as a result of weakness due to migration of a purse-string suture into the cecum
4. Eversion at the stump site as a result of weakness following the rupture of a stump abscess into the lumen of the bowel.

Increased intraluminal pressure and areas of weakness in the cecal wall due to age, congenital causes, epiploic appendages, or the piercing of the wall by blood vessels may also play a role, but are probably not common mechanisms in the cecum.

The gross picture presented is usually a solitary pouch of varying size. The neck may be narrow or wide. Fecaliths are frequently present. Jonas found them in 68.4 per cent of his cases, Baker and Carlile in 54 per cent of the thirty-seven cases they collected, and Beck and Hopkins in three of their five cases. The high frequency of fecaliths may be due to the absence or attenuation of the muscular layer of the diverticulum resulting in insufficient propulsive force to expel feces which enter. A narrow neck may contribute to this.

Varying degrees of inflammation may be present and may extend to the adjacent cecal wall. Ulceration of the mucous membrane and wall of the diverticulum is common, particularly when a fecalith is present. Gangrene with perforation and abscess formation, or even peritonitis may also occur. It must not be forgotten that intestinal obstruction may complicate the picture and carcinoma of the cecum may be associated.

The diagnosis of cecal diverticulitis is not often made preoperatively. In only 6 per cent of Anderson's series of 91 collected and 8 personal cases was the correct diagnosis made before laparotomy. The symptoms and signs are those of an inflammatory process in the right lower abdominal quadrant. They may be indistinguishable from those of appendicitis, which is the common preoperative diagnosis (84 per cent of the cases in Anderson's series). A mass may be palpable, in which case, depending upon the history, a diagnosis of appendical abscess, appendix with omentum wrapped around it, carcinoma of the cecum with or without perforation, carcinoid, foreign body perforation, or cecal granuloma is usual. Diagnoses of salpingitis, degenerated uterine fibroid, chronic cholecystitis, and obturator hernia have also been made, but it is difficult to see how such conditions would be considered except in the most bizarre or unusual cases. When the appendix has been removed, with the exception of the relatively rare stump appendicitis, the conditions referable to the appendix eliminate themselves as possibilities. Carcinoma or granuloma of the cecum then becomes the most common diagnosis, although inflamed omentum or foreign body granuloma have also been considered. In such instances, consideration of the possibility of cecal diverticulitis will result in the diagnosis being made more frequently than has been the experience in the past.

Roentgen examination is sometimes of diagnostic assistance. The plain film of the abdomen may show the presence of a large fecalith, although this may be confused with a foreign body. The barium enema may show a filling defect in the cecal wall, in which case the differential diagnosis from neoplasm must be made at laparotomy. On the other hand, the diverticulum may be actually demonstrated either by the entrance of barium into it or by continuity of the cecal mucous membrane into the neck of a contiguous shadow.

Because of the likelihood of serious complications, diverticulitis of the cecum must be considered a surgical lesion, although conservative treatment, if the diagnosis is definite, has been advised (Schnug). The surgical treatment of choice is simple excision of the diverticulum, with closure of the defect left in the cecum. Even when gangrenous diverticula are encountered, local resection will frequently reveal viable bowel at the resected edges and closure can then be effected without difficulty (Gatewood, Henry). However, the diagnosis frequently has been difficult to make even at laparotomy and, as a result, extensive resections have frequently been performed. This was true in one-third of the cases in Anderson's series. Occasionally, extensive involvement of the cecal wall by an inflammatory and even gangrenous process has been encountered when the correct diagnosis was evident. Or a large inflamed diverticulum lying close to the ileocecal valve or in the mesentery has precluded local excision. In such cases, resection with ileocolostomy, or exteriorization either as a Mikulicz procedure or of the gangrenous portion of the wall alone, has been recommended (Frehling, Jonas). However, in these cases or in those in which the diagnosis is not clear, it would seem much

more logical and certainly safer to perform an ileotransversecolostomy with or without drainage locally as a preliminary to later resection. Naturally if an abscess is encountered, simple drainage is the operation of choice.

The mortality rate in Anderson's series was 6.4 per cent, 4 per cent with diverticulectomy and 9 per cent with resection. With proper appreciation of the pathology and staging of the procedure when resection is necessary, mortality should be reduced to a negligible figure.

CASE REPORT

A. A. (Mount Sinai Hospital No. 616376), a 53-year-old man, was first admitted on Jan. 17, 1950, with a typical story of acute appendicitis of 48 hours' duration. The previous history was irrelevant. The physical findings were also characteristic of acute appendicitis. The white blood count was 12,600 with 84 per cent polymorphonuclear leukocytes and a shift to the left. The abdomen was opened through a McBurney incision. An acute gangrenous retrocecal appendix was found with considerable purulent exudate of the contiguous cecal wall and lumbar gutter which formed the bed of the appendix. A moderate amount of seropurulent fluid was present in the peritoneal cavity. No other pathology was noted. Appendectomy was performed using simple ligation technique with carbolization of the stump. The course was complicated by a wound infection. The wound was opened on the fourth day after operation and foul pus was evacuated. Procaine penicillin and streptomycin were given from the first to the sixth day after operation, and aureomycin from the seventh to the tenth. The patient was discharged on the eighteenth postoperative day with a clean granulating wound strapped together by adhesive tape. He was followed in the Out Patient Department and healing was complete by two weeks after discharge. At follow-up examination on April 6, 1950, the wound was seen to be solid with no evidence of herniation or weakness.

On Sept. 23, 1950, the patient was readmitted with a complaint of abdominal pain of two days' duration. The pain was intermittent and cramping in nature. There had been no nausea or vomiting, and the only change in bowel habits had been seven bowel movements the day before admission after the taking of a cathartic.

The temperature, pulse rate, and respiratory rate were normal, and there were no findings of significance except in the right lower quadrant. There, in the vicinity of the scar of the previous operation, an ill-defined, lemon-sized, tender, somewhat movable mass was palpable. Rectal examination was negative. The white blood count was within normal limits.

A plain film of the abdomen showed a globular density one and three-fourths of an inch in diameter overlying the medial aspect of the right wing of the ilium. By barium enema the density was seen to arise from the medial cecal wall. A small amount of barium had trickled into it and the mucosal folds of the cecum were seen to extend into its mouth (Fig. 1). The terminal ileum was not outlined. The impression was of a large diverticulum. Marked spasticity was observed in the cecum and ascending colon, suggesting the possibility of an engrafted inflammatory process. Multiple diverticula associated with moderate spasticity were scattered along the sigmoid and descending colon.

A roentgenogram of the chest revealed a somewhat homogenous soft infiltration in the right upper lobe of the lung at the level of the first intercostal space anteriorly. A similar smaller infiltration was seen in the left upper lobe. The appearance of these suggested minimal bilateral pulmonary tuberculosis, in view of which the findings of spasticity in the cecum and ascending colon, combined with the failure to visualize the terminal ileum, suggested the possibility of a superimposed tuberculous enteritis.

Laparotomy was performed through a right rectus incision on Sept. 29, 1950. A mass was palpated in the anterior wall of the cecum. The omentum covered this and was adherent to the cecum and the mass. The omentum was dissected free, revealing a lemon-sized mass arising from the anteromedial aspect of the cecal wall about an inch from the ileocecal junction. The mass was a diverticulum about two inches in diameter with a stoma of about three-fourths of an inch. It was subacutely inflamed and filled with hard inspissated feces. No other divertic-

ula were present locally and the cecum was otherwise normal, as were the terminal ileum and the ascending colon. The remainder of the abdomen was not explored. The diverticulum was excised and the opening in the cecum closed with one layer of continuous chromic catgut followed by a second layer of interrupted silk sutures. The wound was closed in layers.

The patient was given procaine penicillin and streptomycin for the first five days after operation. The postoperative course was smooth and the patient was discharged eleven days after operation.

The pathologic report described a saclike segment of large bowel (diverticulum) containing a fecalith. The diverticulum showed subacute inflammation with scarring, and ulceration with acutely inflamed granulation tissue. Microscopically the wall of the diverticulum showed a fairly distinct mucosa in the nonulcerated areas and a well-developed muscularis layer. The mucosa was not mobile, but was bound down to the underlying fibroareolar tissue.

Fig. 1.—Barium enema showing origin of diverticulum (globular density) from medial cecal wall. Small amount of barium seen trickling into mouth of diverticulum (arrow).

COMMENT

The diverticulum in the reported case had a well-developed muscular layer and hence was of the "true" variety. Nevertheless, whether it was congenital or acquired cannot be stated. The presence or absence of a muscular layer has already been shown to be an unsound basis by which to determine this in cecal lesions. Multiple diverticula of the acquired type were present in the left colon, but the large size of this one, its muscular layer, and the absence of other diverticula in the transverse and ascending colon would tend to gainsay a relationship to them. The failure to note its presence at appendectomy

would speak for its genesis subsequent to that operation and, offhand, it is difficult to see how so prominent a structure on the anteromedial aspect of the cecum could have been missed had it been present. However, attention at appendectomy was directed to the prompt delivery and removal of a gangrenous appendix and the diverticulum, not being inflamed at the time, might very well have looked like part of the cecal wall. The site of origin was not the appendix stump, which, it will be remembered, arises from the posteromedial wall of the cecum about an inch below the ileocecal junction, while the diverticulum was located on the anteromedial aspect of the cecum. An etiological possibility in keeping with the mechanisms discussed is production of the diverticulum as the result of traction on the cecum by omentum which became attached to it following appendectomy. It cannot be denied, however, that the converse may have been the case, the omentum becoming adherent to a pre-existing diverticulum only after an inflammatory process had developed therein.

The diagnosis in this case was established preoperatively by roentgenography. When a mass was felt on clinical examination, a foreign body such as a gauze sponge was suggested. This seemed to be borne out by the globular shadow seen in the plain film. However, with the barium enema, the true nature of the shadow was demonstrated.

The surgical treatment here consisted of simple excision. Closure of the cecal defect presented no problem even though the site of origin was fairly close to the ileocecal valve.

SUMMARY

1. The subject of diverticulitis of the cecum is briefly reviewed.

2. A case in which the diagnosis was made preoperatively is presented and discussed.

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LEIOMYOMA OF THE DUODENUM

Case Report and Review of the Literature

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LEIOMYOMA of the stomach is frequently seen, and similar neoplasms of the small intestine are only moderately rare. Primary benign tumors of the duodenum are exceedingly uncommon. In 1937, Le Bigot[1] summarized the literature to that date and found 30 cases of primary benign duodenal tumors including 9 adenomas, 2 hemangiomas, 2 papillomas, 3 myomas, 2 fibromyomas, and 6 "benign" tumors, the pathologic nature of which was not specified. The first report of a benign duodenal tumor in which the pathologic anatomy was described as a leiomyoma was by Hoffmeister[2] in 1935. His patient had a local excision of a tumor 1 cm. in diameter from the wall of the duodenum, with a primary closure and a gastroenterostomy. In 1939, Brechot and associates,[3] reported one leiomyoma and reviewed the European literature, accumulating 8 other cases. In 1945, Hoffman and Grayzel[4] reviewed 64,300 surgical pathologic specimens and 4,480 autopsies, finding 14 benign duodenal tumors. They did not list how many of each pathologic type were found but only stated that adenomas were most common, and included pancreatic rest tumors as another type found in this anatomic location. These authors emphasized that benign duodenal tumors sometimes are incidental findings at autopsy but that melena may be a common presenting complaint. They state that frequently the ulcer syndrome may be mimicked and that if the tumor reaches great enough proportions high intestinal obstruction may ensue.

In December, 1950, a case record of the Massachusetts General Hospital[5] reported a leiomyoma of the duodenum producing massive gastrointestinal bleeding. A local excision of this small tumor was performed.

Assuming "fibromyoma," "myoma," etc., to mean leiomyoma, a total of 15 such cases have been recorded in the literature to date. The following is a case report of another similar tumor:

CASE REPORT

Mrs. E. U. (526333), a 51-year-old white woman entered Presbyterian Hospital Sept. 24, 1951, complaining of abdominal pain occurring intermittently for the preceding 2 years. During this time she had, following meals, dull aching pain in the right upper abdomen, accompanied by nausea but no vomiting. At first these episodes occurred once or twice a week. During the preceding few months, the pain had become more severe, occurring after every meal, and lasting 1 to 2 hours. Because of these attacks she had limited her food intake, but admitted no weight loss.

For 15 years she had been bothered by vague gastrointestinal symptoms, and during this time had never felt perfectly well. Several years previously the stomach had been fluoroscoped elsewhere and was reported to be normal. Eight years previously she had an

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abdominal hysterectomy for menorrhagia, at which time the appendix was also removed. Another doctor had been giving her "shots" for migraine and medicines for anemia. Recent roentgenograms of the stomach and gall bladder were considered negative, but her physician had advised that she have her gall bladder removed. Before doing this she desired another opinion.

She had never noticed radiation of the pain, nor had she complained of hematemesis, tarry stools, jaundice, chills, or fever. Bowel movements occurred daily without laxatives and were well formed and brown in color.

Temperature was 99.6° F., pulse 74, blood pressure 110/78. She was a pale, thin, white woman appearing chronically ill. The head, neck, heart, and lungs were essentially normal. The abdomen was moderately tender everywhere, but was especially so in the right upper quadrant with some spasm there. There was no distention, and bowel sounds were active and of normal quality. The liver, spleen, and kidneys could not be palpated, nor were there abnormal masses felt. Rectal examination was negative. The extremities were negative and there were no palpable lymph nodes.

Fig. 1.—A filling defect in the second portion of the duodenum is demonstrated.

The hemoglobin was 10 Gm., red blood cells 3,490,000, white blood cells 4,600. The blood Kahn test and urinalysis were negative. An Ewald test meal revealed no free acid and a total acid of 45 degrees. There was persistent occult blood in the stools.

X-ray examination (Fig. 1) revealed a normal cholecystogram and colon by barium enema. A stomach fluoroscopy revealed a consistent mucosal deformity from the medial side of the proximal end of the second portion of the duodenum. This finding was present on 3 subsequent examinations and resembled the classic inverted figure 3.

The patient was given 1,000 c.c. of whole blood. On Sept. 9, 1951, the abdomen was opened through a right upper paramedian incision. The gall bladder and liver were adherent to the duodenum and distal portion of the stomach. These adhesions were separated, and the duodenum was mobilized. An encapsulated tumor mass was demonstrated in the second portion of the duodenum, involving its medial aspect, and projecting within the duo-

denal lumen and into the subjacent pancreatic tissue (Fig. 2). The common duct was opened, and a probe was passed into the duodenum. The course of the common duct thereby was outlined and demonstrated to lie below and to the right of the side of the tumor with approximately a 6 mm. margin of normal pancreatic tissue intervening. The distal

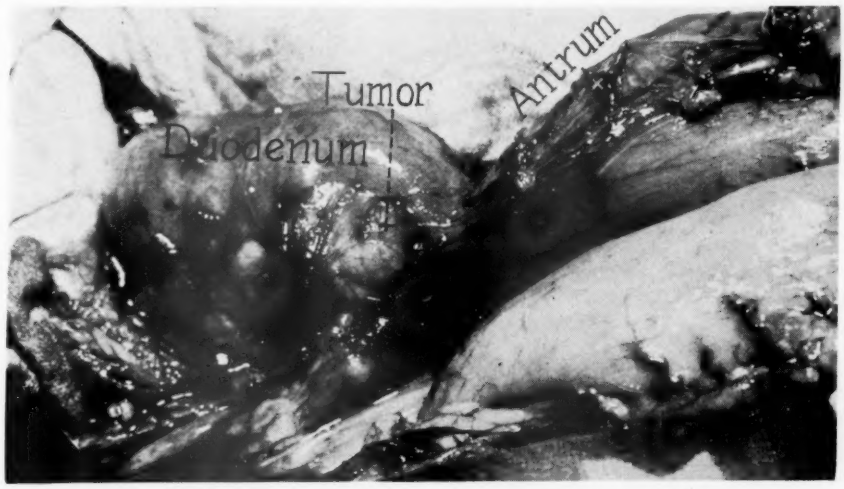


Fig. 2.—The appearance of the duodenal tumor at the time of operation.

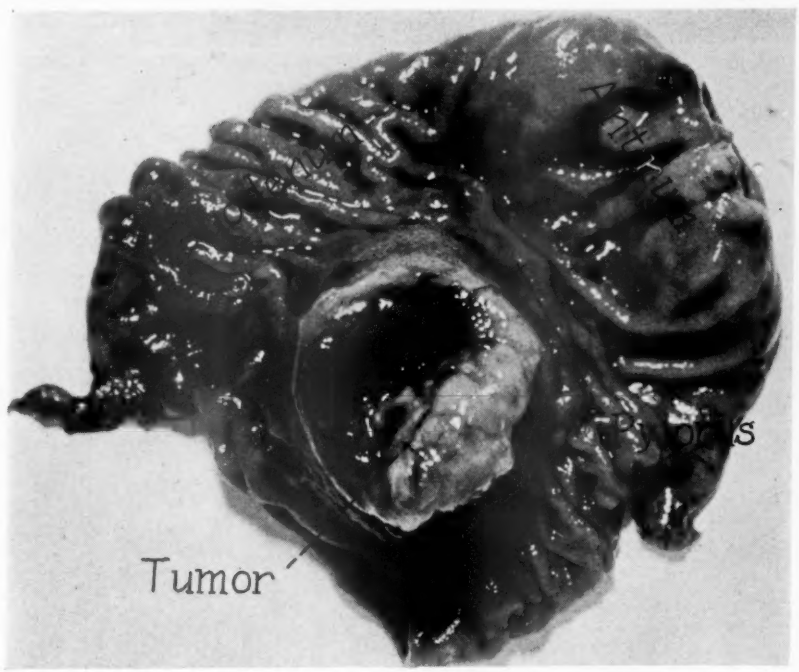
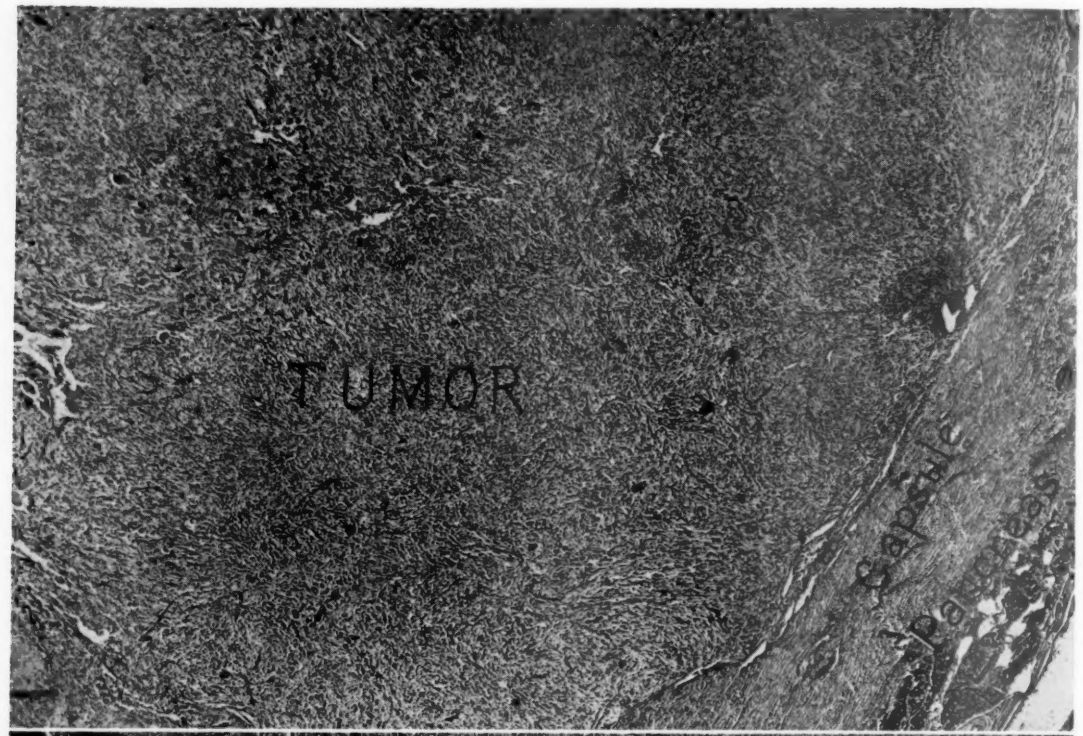


Fig. 3.—The opened surgical specimen.

portion of the stomach was mobilized, separated from its mesenteric attachments, and transected 2 cm. oral to the pylorus. The duodenum was transected 2 cm. distal to the tumor and 1 cm. proximal to the level of the papilla of Vater. The pancreatic tissue surrounding the tumor was divided between hemostats, leaving a ½ cm. margin of pancreatic tissue attached to the tumor capsule. The common bile duct and duct of Wirsung were preserved.

Fig. 4.



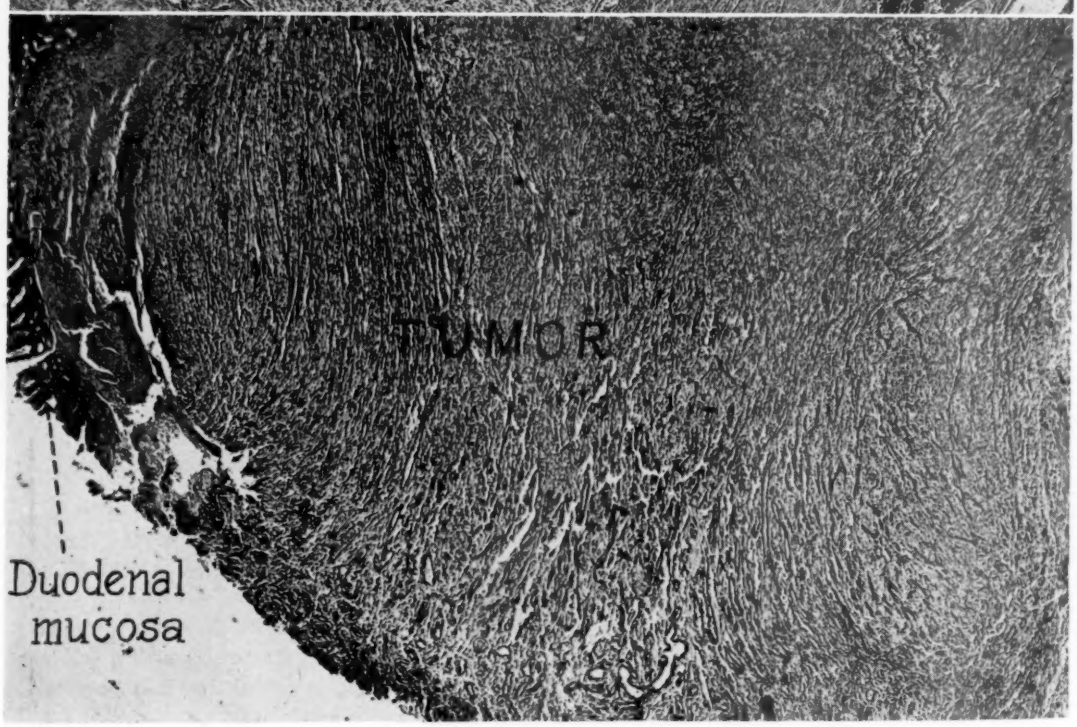


Fig. 5.

Fig. 4.—The microscopic appearance showing the dense capsule and adjacent pancreas (×40).

Fig. 5.—The microscopic appearance near the duodenal mucosa (×40).

An end-to-end anastomosis was performed between the lower end of the divided stomach and the oral end of the transected duodenum. A T-tube was inserted into the common duct and the abdomen was closed.

The specimen (Fig. 3) weighed 38 Gm. and measured 8 cm. in length. It consisted of the distal end of the stomach, the pylorus, and the first portion and part of the second portion of the duodenum. An ulcerated tumor projected 1.5 cm. from the mucosal surface of the medial side of the second portion of the duodenum, 4.5 cm. from the pyloric end. The tumor was 3 cm. in diameter and its lower border was 2.5 cm. from the distal end of the resected duodenum. There was a dense capsule around the serosal aspect of the mass which was surrounded by a rim of pancreatic tissue. Hematoxylin and eosin stains (Figs. 4 and 5) revealed a highly cellular tumor which was fairly well circumscribed and encapsulated and lay in the musculature of the duodenum. The tumor cells encroached upon the pancreatic tissue in one region and penetrated the mucosa at the site of ulceration in another area. These cells were elongated or spindle shaped with a tendency for groups of cells to take on a whorled arrangement and to intertwine. The nuclei were ovoid and rather uniform in size and shape, but occasionally there was a moderate variation in size. In some areas there was a suggestion of palisading. The type of cell and arrangement was most consistent with a diagnosis of leiomyoma.

COMMENT

No history of gastrointestinal bleeding was obtained although laboratory evidence of bleeding was found by stool examination, and a marked anemia existed on admission to the hospital. Other case reports emphasized that melena is the most common symptom. The presenting complaints of pain and nausea following meals can probably be explained by the size of the tumor which probably partially obstructed the duodenal lumen. The preoperative diagnosis of duodenal tumor must be confirmed by careful roentgenologic examination. Such examination may show a filling defect of varying size, usually in the first or second portion of the duodenum. In our case, because of the size of the tumor, duodenal resection seemed to be the treatment of choice. If the tumor is smaller, simple excision will suffice, providing the repair of the wall of the duodenum does not compromise its lumen.

SUMMARY

A case of leiomyoma of the duodenum is added to the 15 such cases found in a review of the literature. The usual symptom complex, the diagnosis, and the treatment of choice are discussed.

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Editorials

The Surgery of Trauma

THE results of injuries impose an ever increasing burden on our nation. The casualties resulting from our military activity are less numerous than those suffered from traffic in the home and industry. Safety campaigns, while of unquestioned value, have not been heeded sufficiently by the public to bring about the expected decrease in the civilian casualty rate. It is, therefore, important that the salvage rate from injuries be increased, not only in regard to life, but also to resulting handicaps.

The surgery of trauma is important in that it serves a large segment of the population at a time when expert help is badly needed. Frequently the early care of trauma patients dictates the type of end result the injured individual will obtain. Evaluation of the condition of the patient and decisions for treatment usually are required promptly.

Nowhere in the field of medicine is the fallacy of dividing the responsibility for the care of the patient into segments based on systemic or anatomic grounds more strikingly illustrated than in the surgery of trauma. Injury is no respecter of specialty interests. If certain automobiles fractured only long bones while others limited their damage to the skull and its contents, and still others showed predilection for the thorax or abdomen, a case might be made for specialty interests and prerogatives in the field of trauma. Even when injuries are limited to a part, it is a whole person who is injured, and the entire patient must be cared for. When multiple injuries are present, the evaluation of the relative seriousness of the injuries, their effect on each other and, more important, upon the patient, must be evaluated on the basis of extensive knowledge and experience.

Interest in special fields has brought about advances within these fields. Recognition must be given to particular skills in the treatment of special problems. The requirements of the injured patient for the application of these skills must be related logically to the entire patient, not through the dictates of limited interest or knowledge. A patient who dies of a ruptured viscus is no less dead because of excellent alignment of the bones of his fractured extremity.

While specialization has aided in the progress of surgery, it has not been all gain. Specialization was born of the particular special interest and enthusiasm of doctors with broad experience. The fathers of the specialties were trained in the tradition of general experience. Commonly their pupils entered the specialty with little of the broad training of their predecessors. Training in the surgical specialties is generally limited, if not entirely devoid, of training in general surgical principles. As specialty training programs have increased, the opportunity for broad training in general surgery has decreased.

Accidents occur fortuitously and respect neither time nor place. Since they require prompt attention, it is important that the principles of the care of trauma be a part of the training of all medical men. The general practitioner sees and cares for more trauma, especially in rural areas, than any other medical group. Any doctor's office may become, at some time or other, a casualty clearing station. In urban areas, severe trauma is more likely to be cared for in large hospitals, especially municipal institutions. Many hospitals with otherwise excellent surgical training programs offer no training in the surgery of trauma. Many do not care to admit or care for trauma patients because of the unpredictable nature and timing of their problems. Hospitals, rural as well as urban, must accept responsibility, not only for the care of injured people, but also for training for the surgery of trauma. Where such programs are not assigned to general surgeons with broad interests and training, all specialty departments must cooperate in the trauma team. Specialty departments, limited in interest and training to anatomic segments, cannot alone be expected to care adequately for injured patients, since injuries are not usually limited, even when they appear so to be.

Training in the surgery of trauma, undergraduate as well as graduate, must consider the injured patient as a whole person and not as a fracture, vascular, neurologic thoracic, or abdominal case. Training, for the surgery of trauma to be effective, cannot be divided into anatomic segments. General surgeons caring for trauma patients must have broad training which includes subjects which overlap into what might be considered specialty fields, and the surgical specialist must have training in general surgery. If the salvage rate of our injured is to be increased, better education in all phases of care of the injured must be made more available.

The responsibility for the care of trauma patients ought to be entrusted to those whose training and experience qualify them to care for the whole patient. Under no circumstance ought the care of injured patients be limited to one group or another on the basis of specialty designations, whether acquired by Boards or by self-labeling. If hospitals feel that they ought to place restrictions on who shall and who shall not care for trauma patients, let it be done on the basis of ability, experience, and a broad knowledge of the care of the injured patient, and not on the basis of labels.

—*Charles G. Johnston*

Notes on the Management of Fluid Balance

IN THE past several years, a number of investigators (Butler, Elman, Winfield, and Fox) have developed polyionic solutions for fluid replacement therapy containing the electrolytes of plasma in about the concentrations found in vivo. These studies have yielded interesting and valuable information in the area of study, and the use of these solutions under controlled conditions, in the hands of capable investigators, has been safe and gratifying. However,

more recently, several commercial drug firms have been marketing so-called "balanced electrolyte solutions" for general use as a multipurpose fluid replacement solution. There is a real danger that promiscuous use of such solutions under uncontrolled circumstances to provide parenterally the fluid and electrolyte requirements of postoperative patients will result again in some patients being literally drowned by excessive salt administration, as occurred in earlier years when normal saline solution was the vogue in fluid replacement.

Since the use of a polyionic solution for parenteral fluid replacement and maintenance therapy has much to recommend it from the point of view of ease and convenience, it could achieve routine practice in some hospitals as suggested in the brochure accompanying the product of one commercial firm. For this reason it is germane to point out the hazards of indiscriminate use of such solutions. Water is not lost from the body as its plasma equivalent, and attempts to meet fluid requirements with a solution containing plasma equivalent electrolytes may result in administering a dangerous excess of such electrolytes.

Many well-documented studies in recent years have established the fact that salt requirements in the immediate postoperative patient are quite low (in the area of 2 to 4 Gm. per day) providing there are no excessive losses of electrolytes by intestinal drainage, external fistulas, or excessive diarrhea. To give 2 to 3 L. daily of a polyionic solution having the electrolyte concentration of plasma will be equivalent to giving 12 to 18 Gm. of NaCl, far in excess of usual requirements. In an individual with limited renal and cardiac reserve such a salt load may precipitate pulmonary edema after a few days. Moreover, the practice of routinely employing a stock polyionic solution for replacement purposes may lead to excessive administration of some particular electrolyte, such as potassium, when its use may prove unnecessary or harmful.

A more rational approach for general purposes, in the light of present knowledge, is to add to the total water requirement of the patient for any particular day, the desired weight or milliequivalents of each individual electrolyte from a concentrated sterile stock solution of each electrolyte. Under such a plan, operating in a hospital where all items of intake and output are accurately recorded, where daily weighing of the patient, as suggested by Wangensteen, is regularly performed, and where reliable blood chemical determinations are available, one can accurately assay the needs of his patient. In this way if sodium, potassium, chloride, bicarbonate, or acetate are needed, they can be added individually to the patient's daily water requirement, which is given as 5 per cent glucose in distilled water, to suit the particular need of the patient and his circumstances.

The problem of fluid and electrolyte balance is still too poorly understood, and blunders are too hazardous, to allow relegation of its management to a hospital routine and to rely upon the patient's kidney to make all necessary adjustments. If the patient's kidneys are in good condition, he has no great need for a good doctor, but if his kidneys are in poor condition, he needs the best medical talent available.

—Arnold J. Kremen

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

PRIMARY CARCINOMA OF THE LUNG

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FEW conditions in medicine have aroused as much interest or assumed as much importance as carcinoma of the lung in such a relatively short time. In a period of only a few decades it has arisen from a comparatively rare and obscure disease to one of the most common forms of malignancy. During this same time, too, and as a result of the pioneering demonstration by Graham[41] that a cancer of the lung could be successfully resected, it has been converted from a hopeless to a curable condition. This was undoubtedly a major factor in generating greater interest in the problem. Despite the rapid development of this intensive interest in carcinoma of the lung the need remains for a wider appreciation of its clinical importance. This is highlighted by the steadily rising death rate from the disease and by the pitifully small number of cases in which the diagnosis is made at a stage when successful therapy can be applied.

The factor deserving perhaps the greatest emphasis concerning this disease is its relative frequency and increasing occurrence. In all parts of the world where the disease has been studied there has been found a steady rise in the occurrence of the disease and it appears to be increasing more rapidly than any other cancer. For example, in this country during the decade ending in 1948 there was a 31 per cent increase in deaths from all types of cancer, whereas deaths from bronchiogenic carcinoma increased 144 per cent.[78] In the British Empire, according to Harnett, the number of deaths from cancer of the respiratory tract increased 120 per cent during the same period in which the total number of cancer deaths increased only 22 per cent. From 1922 to 1947, Doll and Bradford-Hill found that deaths from cancer of the lung in England increased fifteen fold. Official mortality figures in Denmark show a fivefold increase in lung cancer during the 15 year period ending in 1945.[21] Similar observations have been recorded in other countries. This steadily increasing incidence is also revealed by analysis of institutional data derived from necropsy studies as well as admission rates. Virtually all investigators have found that its incidence has progressively increased to the point where it now ranks high

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as a primary form of cancer, comprising as much as 10 to 15 per cent of all carcinomas. In many institutions, including our own, its occurrence now exceeds that of cancer of the stomach.[2, 5, 40, 70]

Much interest and some controversy have developed as to whether this increase in incidence is real and absolute or only apparent and relative and various explanations have been sought to account for this curious phenomenon. Since this phase of the subject has been reviewed previously[76] and for the most part remains speculative, its further consideration here would serve no useful purpose. No matter whether this increasing incidence in the disease is real or only apparent, the important practical fact is the demonstration that the condition is now relatively common. The significance of this fact lies in its influence upon diagnosis. The key to early diagnosis lies in the constant recollection of the possible presence of the disease and this in turn is dependent upon knowledge of its frequency. It has now been well established that carcinoma of the lung is a relatively common disease and accordingly deserves a high index of suspicion.

Carcinoma of the lung is predominantly a disease of the male sex, occurring five or six times more frequently in men than in women. In the most recent analysis of our experience, comprising 948 cases, 89 per cent were found in men. There is some variation, however, in this incidence according to histologic type. Thus, while in the epidermoid and undifferentiated forms of the disease the male sex incidences were 95 per cent and 87 per cent, respectively, in the adenocarcinoma type this figure was only 67 per cent. No satisfactory explanation for this sex discrepancy has been advanced. The problem has been studied experimentally by Kemler and Graham who found that the transplantation of small fragments of human bronchiogenic carcinoma from male subjects was equally successful in both female and male animals and that the administration of sex hormones had little or no effect on the growth.

The age distribution for carcinoma of the lung is similar to that of other carcinomas with the highest frequency in the fifth, sixth, and seventh decades. Approximately 90 per cent of our cases were in these age groups, but the disease is occasionally encountered in both extreme age periods.

Most neoplasms of the lung are malignant and predominantly bronchogenic. There is, however, a small proportion of carcinomas of the lung having both histologic and clinical features that suggest a different origin. Various terms have been applied to this curious form of the disease, including alveolar-cell carcinoma, pulmonary adenomatosis, cystic papillary lung tumor, pulmonary mucous epithelial hyperplasia, carcinosis of the lung, carcinomatoides alveologenica multicentrica, terminal bronchiolar carcinoma of the lung, and diffuse primary alveolar carcinoma of the lung.[25, 42, 45, 50, 59, 79, 84, 91, 95] These variations in terminology reflect the controversy that has developed concerning the origin of these tumors. The evidence would suggest, however, as emphasized by Delarue and Graham, that they are probably derived from alveolar epithelial cells and may have a multicentric origin. An interesting observation concerning this curious type of lung cancer is its resemblance both clinically and histologically to a disease of sheep known as jagziekte, first recognized in South

Africa in epidemic form probably due to a virus.[8, 23, 29, 102] Grossly, two forms of the disease may be recognized: a diffuse type which in the state of so-called gray hepatization resembles lobar pneumonia, and a nodular form with multiple miliary- to marble-sized firm tumor masses that may be discrete or somewhat fused. The lesion is characterized microscopically by alveoli-lined, tall, columnar or large, nucleated, cuboidal mucus-secreting cells many of which show papillary infolding. Clinically, the manifestations may not differ greatly from the more common type of bronchiogenic carcinoma but it differs from the latter in that it occurs in both sexes with equal frequency. It would appear to have a rather wide range of malignancy with a rapid fulminating course on the one hand and a relatively benign course on the other.

Bronchiogenic carcinoma may arise in any part of the bronchial tree and studies of the distribution of the lesion would suggest that the incidence of sites of involvement is a reflection of the relative size of the various segments of the lung. Thus the right lung, which is the larger, is involved somewhat more frequently than the left,[15, 34, 58, 67, 68] the figures in our series being 53 and 47 per cent, respectively. Moreover, in slightly more than half the cases the lesion was situated in the upper lobes, a fact which is of some significance in limiting the diagnostic value of bronchoscopy. Of further significance in this connection is the fact that in somewhat more than a third of the cases (38 per cent) the lesion was situated in the periphery, that is, distal to the lobar bronchi. There appears to be a greater tendency for adenocarcinoma and the undifferentiated forms to arise more peripherally in the bronchial tree than epidermoid carcinoma, an observation made by others.[10, 68] Thus in our series, 51 per cent of the adenocarcinomas were located in the periphery and the comparable figures for undifferentiated and epidermoid carcinomas were 43 per cent and 30 per cent, respectively.

Various classifications of bronchiogenic carcinoma have been proposed based upon the histologic or morphologic appearance of the tumor. The three major groupings which have been used in our cases correspond closely with the classification that is most generally employed.[77] The incidence of these three major histologic types in our 331 resected cases, 49.5 per cent for the epidermoid carcinoma, 30.5 per cent for the undifferentiated type, and 19.9 per cent for the adenocarcinomas, does not differ greatly from that reported by others.[15, 67, 68] Our data, like those of Mason, would suggest that while all of these types occur predominantly in men, in women the relative incidence of adenocarcinoma is higher than the other forms. It would appear, too, that the relative incidence of adenocarcinoma decreases with advancing age, whereas the incidence of epidermoid carcinoma increases with advancing age.

CLINICAL PICTURE

Unfortunately, the clinical picture of carcinoma of the lung, especially in its early stages, is not well delineated, a fact which deserves repeated emphasis. The lack of appreciation of this fact, along with the usually insiduous onset of the disease, and the tendency to disregard the early vague manifestations by attributing them to more common benign factors, such as excessive smoking

or a lingering upper respiratory infection, account for much of the delay in diagnosis. In our experience, as well as in that of others, the most common manifestations are cough, loss of weight, chest discomfort, previous history of upper respiratory infection, hemoptysis, dyspnea, weakness, and wheezing. But these manifestations often occur singly or so vaguely in the early stages that they do not present a characteristic clinical picture. Cough is by far the most common, and usually the earliest, manifestation. It was present in 90 per cent of our cases and it was the earliest symptom in 55 per cent. Because it is so easily attributed to smoking it may be disregarded for some time or until its persistence and the development of other manifestations demand further investigation. The cough is often nonproductive at first but later it is accompanied with expectoration which may become blood-tinged. This is a particularly significant sign, for hemoptysis which varies from blood-tinged sputum to a cupful of bright blood occurred in 55 per cent of our cases.

The history of a previous respiratory infection to which the patient dates the onset of his present complaints is a highly significant manifestation. This was present in 55 per cent of our cases, and was the first manifestation in 22 per cent. It was usually diagnosed as virus pneumonia, nonspecific pneumonitis, influenza, unresolved pneumonia, and the like. The significant feature of this type of onset is that while there may be some subsidence of the acute manifestations, there is an early recurrence or persistence of the symptoms beyond the average time for recovery from such infections. The frequency with which this occurs emphasizes the need for greater awareness of the possibility of carcinoma of the lung as the cause for such manifestations.

Chest discomfort rather than actual pain is a relatively common manifestation occurring in almost two-thirds of our cases. It is often vague and indefinite in the early stages but it assumes special significance if it persists and is accompanied by other manifestations. Loss of weight is a very common finding occurring in about two-thirds of our cases but it is not necessarily an early manifestation. It is progressive, however, and later is associated with weakness. Dyspnea is also not an early manifestation although it is often present by the time the diagnosis has been made. Wheezing which is present in a relatively small proportion of cases may be an early manifestation if the lesion encroaches on one of the lobar bronchi.

There are no characteristic physical findings in the early stages of the disease and the nature of the findings depend upon the site, size, and direction of the growth. If the tumor encroaches upon the lumen of one of the larger bronchi, or on the pleura, rather striking findings may be observed. On the other hand a moderate-sized tumor in the periphery of the lung may be associated with few or no physical findings.

DIAGNOSIS

The most important factor in the diagnosis of carcinoma of the lung is the awareness of its possible presence. Obviously there will be much delay in the diagnosis if it is not suspected and suspicion is less likely to occur if the disease is regarded as rare. As emphasized previously, it has now been well

established that this is a common form of malignancy, even more frequent in the male sex than carcinoma of the stomach according to some observers. It, therefore, deserves early and high consideration as a possible cause of manifestations related to the pulmonary system no matter how vague and indefinite they may be, especially in men over forty years of age.

Roentgenography is by far the most useful diagnostic procedure in providing suggestive evidence of bronchiogenic carcinoma. This is especially true in the early stages of the disease when few or even no manifestations are present. With increasing experience in this problem there is a growing tendency to emphasize the value of this procedure in detecting the earlier or so-called "silent" phase of the disease which may exist for months and even years before producing symptoms. This is supported by the results obtained from mass chest x-ray survey programs. Thus, Scamman reported the detection of 43 cases (7.8 per hundred thousand) of bronchiogenic carcinoma in a series of 563,012 individuals surveyed in this manner and Boucot found 34 cases (21 per hundred thousand) in a series of 156,920. On the basis of results obtained by such surveys, Hilbish has estimated that carcinoma of the lung will be found at the rate of about 10 per hundred thousand. Impressed with the high incidence of lung cancer in apparently healthy workers in industry as demonstrated by such x-ray surveys (0.14 per cent in 40,607 individuals) Boucot suggested that men over 45 years of age should be checked by this means "every 6 months whenever possible." The value of this method of detecting early carcinoma of the lung is further emphasized by Overholt and Woods. These observers found that in 67 patients in whom surgical exploration was done for tumors revealed by chest x-ray surveys—of a total of 7,892 patients—39 (60 per cent) of the tumors proved to be malignant. Particularly significant is the fact that among the patients in their series in whom carcinomas of the lung were found in the asymptomatic phase by survey film and promptly explored, all were resectable with no evidence of lymphatic extension in 70 per cent. On the other hand, among their cases of symptom-producing cancer only 30 per cent were resectable and only 11 per cent of these showed no lymphatic extension. This problem is further highlighted by the recent observations of Abeles and Ehrlich in a follow-up study of 44 patients with single circumscribed intrathoracic densities detected by routine roentgenographic examination. Of 31 cases in this group in which exploratory thoracotomy was advised, it was carried out in 21. In 7 of these a primary malignant lesion was found and in one the lesion was metastatic. In the remaining 10 cases in which operation was advised it was refused by the patient in 3 and by the referring physician in 6, and deferred in one after a negative bronchoscopy although later a malignant lesion was definitely established in this patient. Five of these 10 patients subsequently developed hopelessly advanced carcinoma. Thus of the 44 cases originally observed almost one-third proved to be malignant while in those in which exploration was advised but refused or deferred one-half developed hopelessly advanced cancer. Many other observers have stressed the importance of considering silent lesions detected by routine chest roentgenograms as possibly malignant, especially in men over 40 years of age. This is supported by

the relatively high incidence of malignancy among such lesions following surgical exploration, the reported figures ranging from 12 to 74 per cent.[1, 31, 49, 53, 75, 90, 100]

Thorough roentgenographic examination is also of great value in the diagnosis of suspected cases of carcinoma of the lung and should include fluoroscopy, exposures in various positions, and, where necessary, spot films, grid films, tomography, or the so-called body section techniques. The nature of the roentgenographic findings vary considerably depending upon the site, size, and type of lesion. Abnormal shadows produced by the tumor may result from actual growth and infiltration of the lesion, early partial occlusion of a bronchus with emphysema, and later complete occlusion with atelectasis. This latter occurrence—atelectasis—either segmental or lobar, accompanied by varying degrees of pneumonitis, constitutes one of the most common roentgenographic findings. Earlier, however, a characteristic manifestation is obstructive emphysema, often of a segmental nature, resulting from a relatively small lesion which, during inspiration as the bronchus opens, incompletely occludes the bronchus and permits the passage of air, but during expiration, as the bronchus contracts, completely occludes it and prevents exit of air. Another fairly common but relatively late type of roentgenographic picture is that suggesting lung abscess. This may be the result of necrosis and subsequent infection in a rapidly growing tumor in which there is early proximal bronchial occlusion. The frequency of this type of picture, approximately 10 per cent,[9, 66, 67] emphasizes the need to suspect an underlying carcinoma in any patient over 40 years of age with a lung abscess. Tomographic examination in these cases is of particular value because it provides better visualization of the characteristic irregular "bumpy" features of the cavity wall.[51, 72] Bronchography has not been found of much value, although occasionally, in lesions located in the periphery of the lung or in the upper lobes in which suspicious clinical manifestations exist but ordinary roentgenography discloses insignificant findings, it may be helpful in visualizing obstruction or narrowing of the bronchus. Angiocardiography has recently been proposed by a number of investigators who believe that this means of studying the vascular patterns in the pulmonary field provides useful diagnostic and prognostic information.[6, 28, 56, 73, 93] It is significant that while Dotter and associates found good correlation between their preoperative interpretations of the angiocardiograms and the operative findings they conclude that operation should not be withheld on this evidence. While our experience with this method is limited we doubt that it will prove to be a widely useful diagnostic procedure.

Bronchoscopy is a valuable procedure in supplying information concerning diagnosis and operability, but experience has shown that its usefulness in establishing the diagnosis by means of biopsy is not as great as it was formerly thought to be. In a high proportion of cases bronchoscopic visualization of the tumor permitting a biopsy is not possible because the lesion is located so peripherally or is in the upper lobes beyond reach of the bronchoscopist. Although, earlier, some observers reported incidences of positive diagnosis as high as 60 to 75 per cent, most investigators are now agreed that this is possible in less than one-half the cases. This is well demonstrated by our own experience as

well as that of others. Thus, in a recently reported collected series of 2,138 cases, a positive bronchoscopic biopsy was possible in only 942 (44 per cent) with the figures ranging from 22 to 57 per cent.[4, 5, 16, 22, 32, 43, 52, 55, 58, 68, 83, 94, 100] In our series of resected cases in which bronchoscopic examination was done, a positive biopsy was obtained in 121 (43 per cent).

Another valuable diagnostic procedure is the cytologic examination of the sputum or bronchial secretions, but it requires an experienced cytologist. A thorough consideration of this phase of the subject along with an analysis of an extensive experience has recently been presented in a monograph by Farber and his associates. These authors as well as others[22, 26, 32, 46, 52, 68, 69, 98, 100, 103] who have recently reported their experience provide good evidence of the usefulness of this method of diagnosis which can give a high incidence of positive diagnoses, the figures ranging from about 60 to 90 per cent. In 112 proved cases of bronchiogenic carcinoma in our series a positive diagnosis was obtained by this means in 76 (68 per cent) and a false positive report was made in one case. These results are not as favorable as those reported by some whose experience is more extensive but we are convinced of its value as a supplemental diagnostic procedure, especially in cases in which the tumor is beyond the range of bronchoscopic visualization.

Other means of diagnosis, such as aspiration biopsy, cytologic examination of aspirated pleural fluid, or biopsy of a superficial lymph node, may be employed but their value is usually limited to establishing the diagnosis in hopeless cases. We have previously emphasized the undesirability of aspiration biopsy in clinically operable cases because of the demonstrated danger of implantation of tumor cells in the tissues traversed by the biopsy needle. Further evidence of its undesirability is provided by its high incidence of complications, 20 (8.7 per cent) in a series of 231 cases, of which 3 were fatal.[87]

In about a third of the cases, a positive diagnosis cannot be established except by exploratory operation. With increasing experience we, like others,[7, 31, 36, 39, 55, 61, 63, 75, 82, 83, 85, 92, 96] have acquired a growing conviction that exploratory thoracotomy is justified in all cases in which there is suggestive evidence of lung cancer but in which the diagnosis cannot be established preoperatively despite thorough studies. This is especially true in the silent or relatively asymptomatic lesions, as emphasized by a number of observers. Indeed with the more widespread use of routine examination of the chest, and the more frequent detection of asymptomatic lesions by this means, exploratory thoracotomy will be the only means of establishing the diagnosis in a very high proportion of cases.

TREATMENT AND ANALYSIS OF RESULTS

Surgical extirpation of the tumor-bearing lung and regional lymph nodes is the only curative treatment for bronchiogenic carcinoma. Irradiation therapy[15, 48, 97] is of value as a palliative procedure to alleviate symptoms in inoperable cases, and nitrogen mustard[65] is similarly useful for this purpose. With our increasing experience, the criteria of operability have been broadened and we now believe that the indications of definite inoperability are

the presence of distant metastasis, obvious involvement of the trachea or carina, and the presence of malignant cells in aspirated pleural fluid. Involvement of the phrenic or recurrent laryngeal nerves is not, by itself, a definite contraindication to operation for such involvement was present in several of our patients in whom resection proved possible.

The results of our experience with bronchiogenic carcinoma, based upon a series of 948 cases, shows that there are a number of factors influencing prognosis and survival including the extent of growth, degree of malignancy, and the sex and age of the patient. Of the 948 cases, 385 (41 per cent) were obviously inoperable when first seen. Of the remaining 563 considered operable 51 refused surgery and 512 (54 per cent of the series) were explored of which 332 (35 per cent of the series) were resected. While these incidences are somewhat higher than those found in a large collected series, they are comparable to those appearing in the more recent reports which reflect an encouraging trend toward higher incidences (Table I). There was a significant difference between the incidence of resectability in our Charity Hospital patients and in our private patients, the figures being 23 per cent and 43 per cent respectively, reflecting the tendency on the part of the latter group of patients to seek medical attention earlier. There has been a slight increase in the resectability incidence during the 16 year period covered by this study but it has occurred principally in the Charity Hospital series. Despite this slightly encouraging trend, in our experience as well as in that of others, this incidence of resectability is pitifully low and reflects the need for a better appreciation of the problem. This is further emphasized by the fact that only 27 per cent of the operations could be termed a curative resection, the remainder being palliative resections, indicating that the tumor had already extended beyond the lung either to involve the regional lymph nodes or contiguous structures.

The operative mortality for the entire series was 20 per cent, but in recent years it has shown a progressive decline. As might be expected there is a greater potential operative risk in palliative than in curative resections. Their respective mortality rates were 22 and 14 per cent. The operative mortality among these palliative resections, however, has been significantly reduced in recent years, the figures being 63 per cent for the period 1935 to 1941. and 18 per cent for the period 1947 to 1951. Cardiovascular disturbances constituted the major cause of death in the immediate postoperative period, accounting for 45 per cent of the fatalities. These disturbances, along with other constitutional diseases, are common among patients in the age group in which carcinoma of the lung is most frequent. As emphasized previously[24] they represent an unavoidable element of risk which must be assumed in the surgical treatment of this condition unless the criteria of operability are so strictly limited that patients in whom this complication is liable to occur are excluded and thus denied their only chance of life. This risk, however, can be minimized by the close cooperation of a cardiologist in the management of these patients.

Sufficient data have now accumulated to provide reasonably good figures on survival rates in carcinoma of the lung following resection, and an increasing

number of reports on this phase of the subject have recently appeared. Follow-up studies were obtained in all our cases and the data calculated on the basis of the possible period of survival following operation. Analysis of our data reveals that the distribution curve for the survival rate drops rather rapidly within the first year after resection, but by the second year it begins to be stabilized and continues almost as a plateau from the third to the fifth year, the actual figure at this point being 19 per cent. It would appear, therefore, that a patient who lives through the second year after operation has a good chance of being alive at the end of 5 years. Somewhat similar observations have been reported by others, the figures ranging from 7 to 28 per cent with average range of about 18 to 20 per cent.[5, 14, 20, 38, 67, 71, 80, 82, 97]

TABLE I. INCIDENCE OF OPERABILITY AND RESECTABILITY IN PRIMARY CARCINOMA OF THE LUNG

AUTHORS	YEAR	NO. OF CASES OBSERVED	CASES EXPLORED		CASES RESECTED	
			NO.	PER CENT	NO.	PER CENT
Fetter	1943	31	6	19.3	0	0
Adams	1946	157	94	59.8	49	31.2
Cames, et al.	1946	107	21	19.6	12	11.2
Edwards	1946	1,016	173	17.0	70	6.9
Jones	1947	196	66	33.6	39	19.9
Sellors, et al.	1947		246		130	
Brantigan	1948	63	37	58.7	20	31.7
Gagnon	1948	224	86	38.4	49	21.9
Wenzl	1948	120	36	30.0	10	8.3
Lambert	1948	349	70	20.0	25	7.1
Norris	1948	269			30	
Levitt	1948	100	18	18.0	11	11.0
Lindskog and Bloomer	1948	200	72	36.0	33	16.5
Graham	1948	434	251	57.8	101	23.3
Brock	1948	666	125	18.8	75	11.3
Brea	1948	240	88	36.6	47	19.6
Camblos, et al.	1949	115	42	36.5	19	16.5
Liavaag	1949	80	44	55.0	21	26.2
Overholt and Schmidt	1949	721	342	47.4	200	27.7
Mason	1949	1,000	353	35.3	202	20.2
Marcozzi	1949	100	55	55.0	27	27.0
Gibbon	1949	182	125	68.7	76	41.7
Burnett, et al.	1950	527	191	36.2	94	17.8
Ariel, et al.	1950	1,057	141	13.3	49	4.6
Churchill, et al.	1950	681	294	43.2	171	25.1
Strang	1950	120	14	11.6	8	6.6
Rienhoff	1950	502			158	31.5
Moore	1951	370	157	42.4	100	27.0
McDonald, et al.	1951	871	415	47.6	252	28.9
Total*		9,727	3,316	34.1	1,760	18.1
De Bakey, Ochsner, and De Camp	1952	948	512	54.0	332	35.0

*The figures shown for Rienhoff, Sellors, et al., and Norris are not included in the total.

These survival rates for the resected cases may be better appreciated by comparing them with those obtained for the nonresectable cases. The latter group were composed for the most part of more advanced cases, inoperable clinically or nonresectable at exploratory thoracotomy, but there were included some patients who appeared clinically operable but refused operation. They all received some form of palliative therapy such as irradiation, nitrogen mustard, or other chemotherapeutic agents. Only 6.4 per cent of this group

were alive at the end of 1 year as compared with 32 per cent for the resected cases and at the end of 2 years these respective figures were 1.7 per cent and 20 per cent. Only 1 patient in the nonresected group survived 4 years and he died shortly thereafter; no patient in the nonresected group survived 5 years, whereas the survival rate in the resected group at the end of 5 years was 19 per cent.

The status of the growth, particularly whether or not the lesion has extended beyond the borders of the lung, is the most significant factor affecting the prognosis. This is demonstrated by a comparison of the survival rates between patients with palliative and curative resections. Whereas the 5 year survival rate for palliative resections was 10 per cent, the comparable rate for patients with curative resections was 38 per cent. Thus the survival rate for patients with no extrapulmonary extension of the growth at the time of operation was increased almost fourfold. As emphasized previously the fact that even among patients with palliative resections there was a 5 year survival rate of 10 per cent lends support to our conviction that efforts to perform these resections are justified for prolongation of life as well as for symptomatic relief.

Finally, according to our present experience, based upon an analysis of a series of 948 cases, the gross survival rate in primary carcinoma of the lung at the end of five years is 6 per cent. This is a pitifully small salvage rate emphasizing the need for a greater appreciation of the problem. Along with many others[7, 9, 15, 34, 36, 67, 80-82, 97] we have been impressed by the general lack of awareness in the clinical consideration of the disease as evidenced by the discouragingly long period elapsing between onset of symptoms and institution of treatment. In our cases this averaged slightly over 1 year. While the patient is responsible for some of this delay, a good part of it unfortunately must be attributed to the physician who first sees him. Thus, Björk found that of the 8.4 months' average duration of symptoms the patient was responsible for 3.4 and the physician for 5 months. Similarly Gibbon observed that of the average delay of 8 months between onset of symptoms and establishment of the diagnosis, the patient was responsible for 3½ and the physician for 4½ months. This figure can be greatly reduced, and the salvage rate significantly increased, only by a wider recognition of the frequency of the disease and consequently its early consideration in any patient, especially men over 40 years of age with unexplained chest symptoms, and by prompt measures (including thoracotomy) to establish the diagnosis. There is increasing evidence to support the belief that routine chest roentgenography provides the most effective means of increasing the salvage rate by the detection of the disease in its early asymptomatic stage when the lesion is still localized and most favorable for cure. The demonstration of an abnormal shadow by this means demands aggressive action to establish the diagnosis, and, when other measures fail to reveal the exact nature of the lesion, prompt exploration should be done. Under these circumstances the risk of exploration except in the aged and the debilitated may now be considered less than that involved by the consequences of delay. In light of these considerations and the frequency of carcinoma of the lung in

men over 40 years of age there is reason to support the advocacy of routine roentgenographic examination of the chest in this population periodically, perhaps every 6 to 12 months.

SUMMARY

1. The incidence of primary carcinoma of the lung has been steadily increasing during the past several decades until it now ranks high as a primary form of cancer, comprising as much as 10 to 15 per cent of all carcinomas and exceeding the incidence of carcinoma of the stomach in many institutions. It should now be considered a relatively common disease, especially in men over 40 years of age, and should therefore be accorded an early and high place in the diagnostic consideration of diseases referable to pulmonary disturbances.

2. An analysis of the authors' experience, comprising 948 cases, is presented. The lesions may occur in any part of the bronchial tree with about one-half of them situated in the upper lobes and about one-third in the more peripheral areas, a fact which is of some significance in limiting the diagnostic value of bronchoscopy. Histologically the most frequent type is epidermoid carcinoma, comprising about one-half the cases, with about one-third falling into the undifferentiated group and almost one-fifth into the adenocarcinoma group.

3. Emphasis is placed upon the fact that there is no characteristic clinical picture of carcinoma of the lung in its early stages. The failure to appreciate this fact, and the common occurrence of this lesion along with its usually insidious onset and the tendency to disregard the early vague manifestations by attributing them to commoner benign factors such as excessive smoking or a lingering upper respiratory infection, account for much of the delay in diagnosis, averaging one year in our cases. Early diagnosis is therefore dependent upon a greater awareness of its common occurrence and consequently its early consideration as a possible cause of manifestation related to the pulmonary system no matter how vague and indefinite they may be, especially in men over 40 years of age.

4. Among all diagnostic procedures, roentgenography is probably the most useful and the most important because it permits detection of the lesion in its early stage when few or even no manifestations are present. Experience with mass chest x-ray survey programs suggest that this will permit the detection of such lesions at the rate of about 10 per 100,000 population. Although bronchoscopy is of value in supplying information concerning operability and in establishing the diagnosis by means of biopsy, its usefulness is limited by the fact that in a high proportion of cases, well over one-half, the lesion is located beyond the field of bronchoscopic visualization. Cytologic examination of the sputum or bronchial secretions is a valuable supplemental diagnostic procedure, but it requires considerable experience and careful performance.

5. Even in symptom-producing lesions a positive diagnosis cannot be established except by exploratory operation in almost one-third of the cases. In the earlier, silent lesions this incidence will be higher, emphasizing the need for

exploratory thoracotomy in all cases in which there is suggestive evidence of lung cancer but in which the diagnosis cannot be established preoperatively despite thorough studies.

6. Only about one-third of all clinically observed cases of carcinoma of the lung prove to be operable owing primarily to the long delay in diagnosis. In our series of 948 cases, 54 per cent were explored and 35 per cent were resected. Curative resection, that is, when the lesion is still confined to the lung, are possible in only about one-third to one-fourth of the cases, the actual figure being 27 per cent in our series.

7. The most significant factor affecting prognosis is the status of the growth, that is, whether or not the lesion has extended beyond the confines of the lung. This is exemplified by a comparison of the 5 year survival rate in patients with palliative resections, in which there is extrapulmonary extension of the lesion, with that in patients with curative resection. These figures in our series were 10 per cent and 38 per cent, respectively. For all the resected cases the 5 year survival rate was 19 per cent, but for the entire series of 948 cases it was only 6 per cent.

8. There is increasing evidence to support the belief that routine roentgenographic examination of the chest provides the most effective means of increasing the salvage rate by the detection of the disease in its early asymptomatic stage when the lesion is still well localized and most favorable for cure. The demonstration of an abnormal shadow by this means demands prompt and thorough studies to establish the diagnosis, including exploration if other measures fail to reveal its exact nature. The frequency of carcinoma of the lung in men over 40 years of age, its ready detection by x-ray examination in its early asymptomatic stage, and its high curability in this stage support the advocacy of periodic—perhaps every 6 to 12 months—roentgenographic examination of the chest in this population.

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SURGICAL MEASURES AS SUPPLEMENTS TO THE MANAGEMENT OF IDIOPATHIC ULCERATIVE COLITIS; CANCER, CIRRHOSIS, AND ARTHRITIS AS FREQUENT COMPLICATIONS

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THE management of idiopathic ulcerative colitis is a trying and treacherous problem in any hands, and the source of much difference of opinion. In a study period of seventeen and one-half years, ending June 30, 1951, 267 cases were seen for therapy and study at the University of Minnesota Hospitals and the Minneapolis General Hospital. It is the purpose of this paper to summarize the results and lessons in that period.

FATE OF PATIENTS WITH IDIOPATHIC ULCERATIVE COLITIS WHO DO NOT HAVE SURGERY

As Table I shows, 102 patients had no definitive surgery for ulcerative colitis. This group includes also those in whom such surgery was deferred, often under intensive medical therapy, until the situation had become desperate, as by perforation and peritonitis, or by cirrhosis and ascites. It is true that many of these patients did not have consistent, good, prolonged, medical management. Follow-up was difficult, and short in many cases. Inspection of the table shows that over one-half of the total followed patients died of colitis or direct complications thereof (cirrhosis, colon cancer, thrombotic development, etc.), and over two-thirds of the group died of all causes.

FATE OF PATIENTS WHO HAVE HAD DEFINITIVE SURGERY FOR IDIOPATHIC ULCERATIVE COLITIS

As Table II shows, 159 patients have had definitive surgery for chronic ulcerative colitis, including ileostomy, colectomy, vagotomy, and other appropriate operations.† *Twenty per cent of those patients who were satisfactorily*

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†The operative care of these patients in this study period was initiated by Dr. M. H. Manson and Dr. W. T. Peyton, who relinquished it to Dr. John R. Paine. Dr. Paine assumed the major share of the burden from 1938 to 1941. Since 1941, the authors and Dr. O. H. Wangensteen have dealt with the vast majority of these cases. In the entire study group, 121 of these cases have been operated upon by one or both of the authors. The six patients not listed in Table I or Table II had had definitive surgery elsewhere before coming here.

TABLE I. FATE OF 102 PATIENTS NOT UNDERGOING SURGERY FOR COLITIS, 1934-1951

	TIME FOLLOWED FROM BEGINNING OF OBSERVATION AT UNIVERSITY HOSPITALS					
	0 TO 12 MONTHS	1 TO 4 YEARS	5 TO 9 YEARS	10 YEARS AND OVER	TOTAL	COMMENT
Patients followed						
Alive	3	6	3	3	15	4 of 15 patients apparently had arrested CUC
Dead	24	10	1	2	37	10 of 37 deaths unrelated to CUC
Patients lost to follow-up*	20	19	7	4	50	5 of 50 cases apparently arrested when last seen

*Not followed since Jan. 1, 1950.

followed died, all of colitis, complications thereof, or surgical catastrophes. These data are based on all definitive operations in the study period. Restriction of consideration to procedures recommended in the light of this paper, i.e., vagotomy where indicated, without previous attack on the intestine (no deaths in 28 cases), primary colectomy and ileoproctostomy, where indicated (no deaths in 23 cases), and primary colectomy and ileostomy (one death in 30 cases), has resulted in a surgical mortality rate of less than 5 per cent (1.23 per cent). The loss rate in this group to the end of the study period was about 5 per cent (4.92 per cent).

TABLE II. FATE OF 159 PATIENTS* UNDERGOING SURGERY FOR COLITIS, 1934-1951

	TIME FOLLOWED FROM BEGINNING OF OBSERVATION AT UNIVERSITY HOSPITALS					
	0 TO 12 MONTHS	1 TO 4 YEARS	5 TO 9 YEARS	10 YEARS AND OVER	TOTAL	COMMENT
Patients followed						
Alive	16	59	29	3	107	97 patients well or with disease arrested
Dead	14	10	2	0	26	11 surgical deaths, 15 deaths due to complications of colitis
Patients lost to follow-up†	12	12	2	0	26	16 patients well or with disease arrested when last seen

*Patients in nonsurgical and surgical groups total 261. Six patients operated upon elsewhere not included.

†Not followed since Jan. 1, 1950.

IDIOPATHIC ULCERATIVE COLITIS AS A PRECANCEROUS LESION

The most serious complication of chronic ulcerative colitis is carcinoma of the colon. In reports of series of cases in the literature, up to 5 per cent of patients with ulcerative colitis have developed carcinoma.[9, 15] A paper from this clinic cites a 14 per cent incidence in patients keeping their colons after 5 years from the time of onset of colitis.[6] Various series have reported the age of occurrence of carcinoma to be between the ages of 39.3 years and 44.3 years, much earlier than in those without colitis. The duration of ulcerative colitis before carcinoma is diagnosed has varied in these series from 2 years to 49

years. The seriousness of this complication is emphasized by the fact that there were 88 per cent and 93 per cent mortalities in 2 reported series of carcinomas secondary to colitis.[10, 19]

During the period of this study, it has been possible to evaluate the likelihood of the development of carcinoma in 263 cases. Each case has been classified on the basis of the duration of colitis in the colon. In the remaining 4 cases there is no record of the time of onset of colitis.

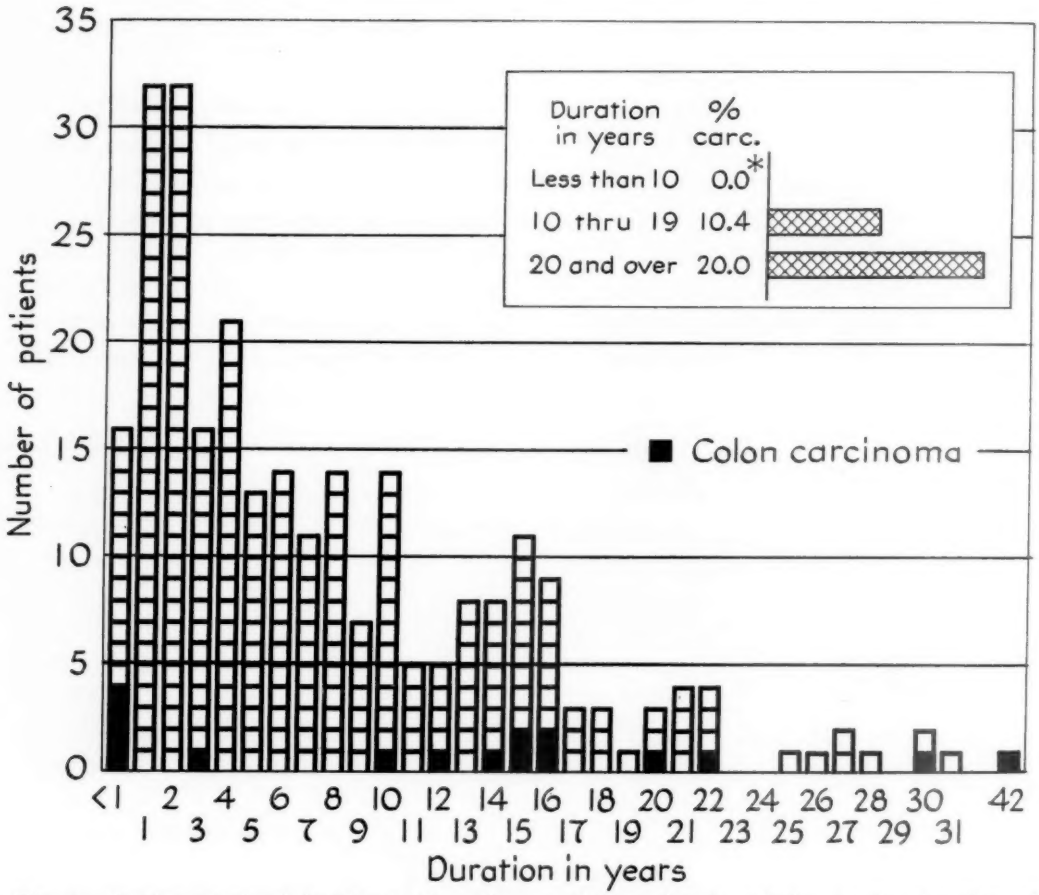

Fig. 1.—Scatter graph of incidence of carcinoma of the colon in relation to the duration of idiopathic ulcerative colitis.

*The four carcinomas occurring at less than one year and the one at three years are interpreted as not due to previous colitis. Those in the first year were obstructing cancers of the descending colon with pathologically diagnosed colitis above, extending only a few centimeters. That at three years developed in a colon afflicted with both colitis and polyposis.

In those patients having chronic ulcerative colitis as the primary disease, the earliest carcinoma appeared 10 years after symptoms of colitis had begun. During subsequent years, 10 other patients developed cancer, a total of 11 cases out of 263, or 4.2 per cent. However, in those who have had the disease over 2 years, the incidence is 6 per cent, and in those over 20 years, 20 per cent. It appears that the incidence of cancer in those patients having suffered the disease for many years is an increasing and very sizable factor in calculat-

ing their prognosis. The data available in Fig. 1 are consistent with the thesis that each patient leaving his colon in place runs about 1.6 per cent risk of developing cancer in that colon in each year over 9 years in which he retains within his abdomen a colon involved with idiopathic ulcerative colitis.

In 70 patients the rectum was not removed at the time of the colectomy because it was normal, because it was minimally involved and deviation of the fecal stream was expected to permit improvement, or because the status of the patient did not permit pancolectomy in 1 stage. Those patients with normal or nearly normal rectums usually had ileoproctostomies performed, and those with severely diseased rectums were given terminal ileostomies, usually with inversion of the rectal stump beneath the peritoneal reflection. All of these patients were advised to return at frequent intervals for proctoscopic examination of the remaining rectal segment, and many were advised to have the rectum removed for persistence of proctitis or suspected premalignant changes. Two patients developed carcinoma in the rectal segment subsequent to colectomy. One of these patients had refused proctectomy for one year after it had been advised. The second patient had neglected to return for proctoscopic examination for 4 years after ileoproctostomy.

Development of pains, obstruction, increase in frequency, and appearance of blood or mucus in stools are not recognized as symptoms of carcinoma in patients with idiopathic ulcerative colitis, and early carcinomas are therefore usually overlooked. Furthermore, the rigidity of the colon makes roentgenologic diagnosis of carcinoma by barium enema extremely difficult. One of our patients died of carcinomatosis 6 weeks after having a barium enema which, while showing the obvious colitis, failed to reveal evidence of malignancy in the colon (See Fig. 2).

Of the 11 patients developing carcinoma secondary to chronic ulcerative colitis, 3 are alive. One of these has carcinomatosis. The other 2 are free of evidence of recurrent colic cancer on "second look" laparotomy[12] some months after removal of the lesions.

NONNEOPLASTIC COMPLICATIONS OF IDIOPATHIC ULCERATIVE COLITIS

The complications of ulcerative colitis other than carcinoma are tabulated in Table III. Ninety-eight patients (36.7 per cent) had these complications. Twenty-nine patients (10.9 per cent) had multiple complications. Thirty-two (12.0 per cent) died of nonneoplastic complications. Of those with arthritis, all but 1, who already had some joint fusion at the time of colectomy, improved following removal of the colon, and most have enjoyed complete loss of symptoms.

VAGOTOMY IN THE MANAGEMENT OF IDIOPATHIC ULCERATIVE COLITIS

Since October, 1946, 40 vagotomies have been done in this department for idiopathic ulcerative colitis or complications thereof. The last report is that of Eddy, which carried the follow-up period to the fall of 1949.[8]

Tables IV and V present the pertinent data concerning these patients. As Table IV shows, 28 patients have had vagotomy done as the initial surgical

B.

A.

Fig. 2.—Masking of signs of gelatinous adenocarcinoma by idiopathic ulcerative colitis. Barium enema roentgen studies of the colon of Case 610254. *A*, At age 16 (12 years of colitis) there is remarkable shortening of the left colon and fibrosis of the entire colon. *B*, Four years later, showing no striking change except that ileostomy has been done. Nevertheless, the patient was dead of carcinomatosis from a carcinoma of the descending colon 6 weeks later.

TABLE III. NONNEOPLASTIC COMPLICATIONS OF IDIOPATHIC ULCERATIVE COLITIS

	NO. OF CASES		PER CENT	
Perforation of colon		10		3.7
Peri-anal abscess		8		3.0
Fistula in ano		4		1.5
Rectovaginal fistula		3		1.1
Ileocolic fistula		2		0.8
Massive hemorrhage*		4		1.5
Liver abnormalities†		50		18.7
Cirrhosis	12		4.5	
Atrophy	2		0.8	
Lesser abnormalities	14		5.2	
Abnormal function tests	22		8.2	
Arthritis‡		19		7.1
Thromboembolic disease		20		7.5
Fatal pulmonary embolism	10		3.7	
Pyoderma		9		3.4
Cholelithiasis		6		2.2
Nephrolithiasis		3		1.1

*One fatal.

†Six patients (2.2 per cent) died of liver failure. A report on liver biopsy is in preparation with Dr. F. W. Hoffbauer.

‡Ninety-two per cent having surgical therapy improved after operation.

step, but 9 direct attacks on the bowel have been required subsequent to this operation. Seven of these procedures were colectomy with either ileostomy or ileoproctostomy, done because of fear of cancer; no cancer was found. Two patients have been colectomized because the disease progressed unabated.

Three patients, 2 of whom also have had colectomies, have been subjected to pelvic parasympathectomy, the method for which is based upon the anatomic studies of Lannon and Weller.[11] In 1 of these patients, there was no response apparent. The other 2 have become symptom-free and proctoscopically negative. One of these, Case 36, developed gastric retention after vagotomy, which required gastroenterostomy. A stomal ulcer, which had then developed, healed after ileostomy. After one-stage pelvic parasympathectomy, colectomy, and ileoproctostomy, the patient's general status, proctoscopic appearance, and bowel habits were all excellent.

It is noteworthy that only 1 instance of severe acute flare-up has occurred after vagotomy in these 28 patients.

The data presented in Table IV have been very critically gathered and evaluated in an effort to provide a basis for prognostication of the effect of division of the vagi in prospective cases. The single item which seems of most importance is that of the degree of fibrosis in the wall of the bowel. Next in order of importance are gross hemorrhage and extent of ulceration. The soundest basis for recommending vagotomy lies in use of it for patients with minimal fibrosis who do not have a history of more than 2 or at the most 3 years of the disease. Some patients who satisfy these criteria, but who present marked gross bleeding or extremely extensive ulceration, should be excluded from the candidate group or conceivably submitted to a preliminary ileostomy (Case 12, Table V). It is incumbent on the surgeon to watch these patients critically, for the risk of late cancer development is as yet unknown.

TABLE IV. EVALUATION OF PATIENTS UNDERGOING VAGOTOMY

EDDY CASE NO.	DURATION DISEASE PREOP. (YR.)	FIBROSIS	GROSS HEMORRHAGE	EXTENT ULCERATION	STATUS AT TIME OF VAGOTOMY	TOTAL PERIOD FOLLOWED (IN MO.)
2	13	0	0	1+	Fulminating, chronic	33
3	5	0	0	0	Acute, chronic	34
4	15	0	0	0	Chronic	47
5	6	0	0	0	Chronic	55
7	2	2+	1+	2+	Chronic	48
9	4 mo.	0	0	0	Acute	25
11	6	2+	0	1+	Chronic	44
14	2 mo.	0	0	2+	Fulminating	47
15	10	0	2+	0	Acute, chronic	24
18	5	4+	0	0	Chronic	45
20	6	4+	4+	2+	Chronic	37
23	1	0	4+	0	Fulminating, chronic	44
24	2	3+	0	0	Chronic	1
25	2	1+	0	2+	Acute, chronic	43
26	3	1+	1+	2+	Acute, chronic	42
27	2	0	2+	1+	Acute, chronic	38
28	9	0	0	1+	Acute, chronic	20
30	2 mo.	0	2+	1+	Acute	7
32	3	2+	0	0	Acute, chronic	34
33	1	2+	2+	1+	Acute	21
34	10 mo.	0	1+	2+	Acute	28
35	1	0	2+	0	Acute, chronic	30
36	3	0	2+	1+	Acute, chronic	29
38	2	4+	0	1+	Acute, chronic	5
39	5	1+	0	1+	Acute, chronic	25
40	5 wk.	1+	1+	1+	Acute	23
41	1½	4+	0	3+	Chronic	26
42	5 wk.	0	2+	2+	Fulminating	11

*Two cases (29 and 37) omitted because only 1 month follow-up. Both were clinically improved at that time, but both refused re-examination, and both refused to return.

†Died of pulmonary embolus following colectomy after end of study period.

WITHOUT PREVIOUS DEFINITIVE INTESTINAL SURGERY*

RESULT AFTER VAGOTOMY			FURTHER SURGERY	FINAL STATUS
CLINICAL	PROCTOSCOPIC	X-RAY		
Symptom-free	Negative	Improved		Symptom-free
Symptom-free	Improved	Unchanged		Symptom-free
Symptom-free	Negative	Improved		Symptom-free
Symptom-free	Negative	Negative		Symptom-free
Unchanged		Unchanged		Unchanged
Symptom-free	Negative	Unchanged		Symptom-free
Improved	Improved	Progressive	Colectomy (proc. or x-ray suggest. of ca.)	Improved
Symptom-free	Negative	Negative		Symptom-free
Improved	Improved	Negative		Improved
Unchanged	Unchanged	Unchanged		Unchanged†
Improved temporarily	Improved	Unchanged	Colectomy (proc. or x-ray suggest. of ca.)	Symptom-free
Improved	Improved temporarily		Pelvic parasympathectomy; no improvement; pancolectomy	Symptom-free
Improved	Improved	Unchanged		
Symptom-free	Negative	Improved		Symptom-free
Symptom-free	Improved	Improved temporarily		
Improved	Improved		Completion vagotomy	Symptom-free
Symptom-free	Negative		Colectomy (proc. or x-ray suggest. of ca.)	Symptom-free
Improved	Unchanged	Unchanged		Improved
Symptom-free	Negative	Progressive	Colectomy (proc. or x-ray suggest. of ca.); terminal ileac progression; colon healed; incom. vagotomy; colectomy and ileoproctostomy	Symptom-free
Unchanged	Unchanged		Pelvic parasympathectomy; thereafter proc. negative	Symptom-free
Improved	Improved	Worse	Colectomy; ileoproctostomy for progressive colitis and acute arthritis	Improved
Improved	Improved		Colectomy (proc. or x-ray suggest. of ca.)	Symptom-free
Unchanged	Unchanged	Worse	Colectomy (proc. or x-ray suggest. of ca.); gastroenterostomy; stomal ulcer; ileostomy, pelvic parasympathectomy, ileoproctostomy; now proc. negative	Symptom-free
Improved	Unchanged	Unchanged		
Symptom-free	Negative	Improved		Symptom-free
Improved	Improved	Unchanged		Improved
Unchanged	Unchanged	Unchanged	Colectomy (proc. or x-ray suggest. of ca.)	Symptom-free
Improved temporarily	Improved			Died in other hands; malnutrition, liver failure

TABLE V. VAGOTOMY AFTER PREVIOUS DIRECT SURGERY ON THE BOWEL*

EDDY CASE NO.	PREVIOUS SURGERY	INDICATIONS FOR VAGOTOMY	RESULT
1	Excision of all gut from anus up to 6 feet from ligament of Treitz	Enteritis	Much improvement
6	Colectomy and ileosigmoidostomy	Proctitis, enteritis	Much improvement; symptom-free
8	Colectomy and ileostomy	Possible enteritis	Equivocal improvement
10	Colectomy and ileostomy (elsewhere)	Proctitis	Refused examination; died elsewhere of intestinal obstruction
12	Ileostomy	Colitis and proctitis	Healed completely; ileostomy closed; well 3½ yr. after
13	Colectomy and hemi-ileectomy and ileostomy	Possible enteritis	Improvement No change
16	Ileostomy and anal pull-through	Diarrhea	
19	Ileostomy	Rectal discharge, sepsis	Died 8 mo. postop.; autopsy showed mid-ileosigmoid fistula
21	Colectomy and ileoproctostomy	Proctitis, enteritis	Healed
31	Colectomy and ileoproctostomy	Proctitis, enteritis	Improvement

*Have omitted from Table V 4 cases listed by Eddy: Case 7, not colitis, Case 22 vagotomy not accomplished, Cases 29 and 37, no return.

Table V is a presentation of data concerning those 10 patients who had had some direct surgery upon the intestine prior to the performance of vagotomy. The indications and results suggest that there are distinct possibilities in this connection.

OPERATIONS ON THE INTESTINE IN IDIOPATHIC ULCERATIVE COLITIS

Choice of Procedure

In the past, the general policy of surgeons dealing with the colon in idiopathic ulcerative colitis lay in the performance of an ileostomy as the initial procedure, followed, after a period, and upon appropriate indication, by colectomy, staged or otherwise.[2] The high incidence of cancer as a complication of colitis, together with the still higher incidence of liver damage and other serious complications, has led us to recommend colectomy in virtually all cases with sufficient disease to justify ileostomy. Trial was given to left hemicolectomy in 3 cases with involvement apparently limited to this area; in each of these cases the right colon subsequently developed marked disease and was therefore also removed. In the presence of proctoscopic and roentgenologic evidence of advanced disease, freedom from marked symptoms is but a setting for cancer development, and should not be a basis for delay.

Throughout most of the period under study, ileostomy has been undertaken as a separate initial procedure. In 74 cases, there were 8 deaths directly attributable to performance of ileostomy—a 10.8 per cent mortality rate,—and 8 additional deaths occurred for other reasons (Table VI).

Elective colectomy some months after ileostomy has been found in our experience to be associated with almost no mortality—but 1 death in 61 cases,—but colectomy with either ileostomy or ileoproctostomy as the initial, one-

TABLE VI. MORTALITY OF ILEOSTOMY AS A SEPARATE INITIAL PROCEDURE

Total separate initial ileostomies		74
Surgical deaths		8
Pulmonary embolism	2	
Hiccups, procaine block, pneumothorax	1	
Torsion of ileum around gut going to ileostomy		
Early	1	
Late (4 months)	1	
Fecal fistula, liver failure (3 months)	1	
Involvement of entire gut and stomach	1	
Coronary occlusion	1	
Other deaths		8
Jejunosigmoid fistula, unsuspected (death at 8 months)	1	
Death while preparing to open abdomen for ileostomy	2	
Late cancer of colon	2	
Cirrhosis of liver	2	
Late massive hemorrhage from colon	1	

stage procedure, as recommended by Wangensteen and Toon,[16] is similarly safe—1 death in 55 cases (Table VII). By application of the single-stage principle, therefore, the risk of accomplishing ileostomy and colectomy has dropped from at least 12 per cent (10.8 per cent for ileostomy plus 1.6 per cent for late colectomy) to less than 5 per cent (1.8 per cent in this series). Evaluation of cases presents little evidence of selection in application of one-stage ileostomy and colectomy as against ileostomy alone; in fact initial colectomy has repeatedly been successfully employed in critically ill patients, with far less postoperative morbidity than we have seen after ileostomy alone.

TABLE VII. RISK OF RESECTIONS AND ASSOCIATED PROCEDURES*

		DEATHS (SURGICAL)		
		NO.	PER CENT	CAUSE
Subtotal colectomy† after preliminary ileostomy	29	0	0	
Total colectomy including rectum after preliminary ileostomy	14	0	0	
One-stage subtotal colectomy and ileostomy	17	1	5.9	Pulmonary embolus in 8-year-old boy; second such case occurred after end of study period (see Table IV)
One-stage pancolectomy including rectum and ileostomy	13	0	0	
Colectomy and ileoproctostomy after preliminary ileostomy	16	1	6.3	Pelvic abscess 2 mo. postop.; died 3 mo. postop. in spite of ileostomy
One-stage colectomy and ileoproctostomy	23	0	0	
Ileoproctostomy after previous colectomy	4	0	0	
Ileo-anal "pull-through" operations; 3 of the 4 were later shown to have been done with involved ileum; all 4 terminated with permanent ileostomy	4	0	0	
One-stage 2				
After prev. ileostomy 2				
Proctectomy	24	0	0	
Total	144	2	1.4	

*There is one surgical death not presented here or in previous tables. This patient came to University Hospitals after ileostomy elsewhere had been followed by proximal ileac perforation and widespread peritonitis.

†To pelvic peritoneal floor with closure of rectum.

The outlook for patients with ileostomy after accomplishment of colectomy is the best of any group to receive treatment of any kind for idiopathic ulcerative colitis (Table VIII). The vast majority has been able to resume normal pursuits in life. Four of these patients have borne children uneventfully since colectomy, albeit 3 by cesarean section.

TABLE VIII. FOLLOW-UP DATA ON PATIENTS WITH ILEOSTOMY AND COLECTOMY; PERIOD OF FOLLOW-UP AFTER REMOVAL OF COLON

FOLLOW-UP (YR.)	NO. OF PATIENTS LIVING AND WELL	LIVING BUT ILL		NO. DEAD*
		NO.	CONDITION	
0	18	1	Under psychiatric care	2
1	15	1	Under psychiatric care	0
2	8	1	Perineal ileostomy attempted before abdominal ileostomy; persistent excoriation from segment of ileum not yet removed	1
3	4	0		0
4	7	1	Severe polyarthritis, established before colectomy, has continued to present since colectomy	0
5	6	0		0
6	4	0		0
7	1	0		0
8	2	1	Lost all colon, ¾ small intestine; pseudomucinous cystadenomatosis	0
9	2	0		0
10	1	1	Lost all colon, ¾ small intestine	0
	69	6		3

*All three deaths due to carcinomatosis from cancers of involved colon which had metastasized before colectomy.

Wangensteen and Toon also suggested that removal of most of the diseased bowel should prove of sufficient benefit to permit anastomosis of the terminal ileum to a 12 to 15 cm. remnant of rectum. This procedure has been evaluated during this study period in 41 cases. It is apparent from inspection of Table IX that the over-all risk of employment of this measure is considerable in terms of mortality and morbidity, in rather marked contrast to ileostomy and colectomy. It is nevertheless tenable that careful selection of cases, and inclusion of those who refuse ileostomy, justify employment of ileoproctostomy in a modest share of patients.

TABLE IX. RESULTS OF COLECTOMY AND ILEOPROCTOSTOMY

Present status:		
5 or fewer formed stools		19
6 or more stools or liquid stools		16
Catastrophes		6
Perforation of suture line and pelvic peritonitis 2 months postoperatively (1946); death	1	
New cancer in rectum after 4 years; death	1	
Recurrent cancer; death	2	
Recurrent severe proctitis; death	1	
Recurrent severe proctitis; ileostomy	1	
Proctoscopic picture in those examined:		
Reversion to "negative"		6
Increase in activity		11
Inactive at present time		15

Certain additional data are of importance in the choice of ileoproctostomy. In three patients in whom proctitis developed after anastomosis, the rectum improved a great deal after performance of transthoracic vagotomy, and in one the rectum healed completely after pelvic parasympathectomy in addition to vagotomy. In 2 patients the rectum improved and in 1 patient involvement of the small intestine disappeared following prolonged employment of Banthine. One patient developed ascending enteritis concomitantly with a recurrent carcinoma obstructing the anastomosis, and the high grade obstruction appeared to contribute to the enteritis.

Techniques of Operations on the Bowel in Idiopathic Ulcerative Colitis

Ileostomy-colectomy.—In the therapy of idiopathic ulcerative colitis, ileostomy alone has been abandoned by the group at the University of Minnesota. In other diseases in which ileostomy may be unavoidable, we have come to feel that a loop ileostomy is preferable to a single-barrel one by virtue of minimization of ileus secondary to handling and adhesions of ileum. The lower stoma should be the discharging stoma, and careful anchorage to the posterior rectus sheath is imperative.[5]

In performance of ileostomy and colectomy, the abdomen is opened through a left paramedian incision 3 cm. from the midline and running from the pubis to a point midway between the umbilicus and the costal margin. The ileum is divided between clamps 2 to 3 cm. from the cecum or at the upper margin of grossly evident disease, and a 1 cm. segment is sent to the pathologist for rapid frozen section and study. If there is no gross evidence of ileac involvement, and no evidence of cancer in the right colon has been found at any time, the surgeon preserves all the mesentery of the ileum, the cecum, and the ascending colon in proceeding with colectomy. If a segment of ileum over 25 cm. long is found involved and will therefore be removed, the right colic vessels may more simply be secured and divided close to the origins thereof, while still leaving sufficient mesentery free for the later formation of a lateral diaphragm (see below). As soon as the pathologist's report on frozen section is made, attention is returned to the ileum, removing 6 to 7 cm. at a time, until no evidence of submucosal cellular infiltration appears. The remaining end of ileum is closed by a catgut Parker-Kerr stitch, which is cut off without tying as soon as closure has been reenforced with 3 or 4 Halsted mattress sutures of silk. Time is conserved by continuing with colectomy during preparation of frozen sections.

No effort is made to close the lateral gutters. The superior hemorrhoidal vessels are preserved if adequate preliminary proctoscopic examination has shown no sign of cancer. If the rectum is to be removed, dissection downward from the low sigmoid level is performed immediately adjacent to the muscularis of the rectum to a point 6 or 7 cm. from the perineal skin, the bowel is tied by ribbon, cut, and cauterized. The pelvic peritoneum is closed with silk.

After ileostomy is completed, the patient is placed in lithotomy position. The rectum is irrigated until clean, and then removed with a finger in the lumen

to leave behind all tissue except the rectal wall proper. Closure is accomplished by catgut approximation of the levators, and by subcuticular stitches in the skin. A catheter is left in the posterior space a week for antibiotic irrigations.

If the rectum is to be left in place, it is closed by Parker-Kerr catgut and silk mattress sutures just below the peritoneal reflection.

Ileostomy is made in the belt line 3 to 4 cm. to the right of the midline and no closer than 5 cm. from the umbilicus. Avoidance of placement of the ileostomy in transverse skin creases is important to later adhesion of the Koenig-Rutzen bag, and may be facilitated by marking creases as the patient leans forward before surgery. A circular incision 2½ cm. in diameter is made through all layers, and ileum and mesentery thereto are sutured to posterior rectus sheath and peritoneum with 12 to 15 sutures of 2½ lb.-test silk. The technique is simpler than previously described[2, 5] in that preplacement of sutures is needed only laterally, as direct exposure on the other 3 sides of the ileum is not difficult through the main incision. The mesenteric margin of ileum is placed laterally in the ileostomy, and suture of the mesentery to the anterior, lateral, and posterior abdominal wall builds a complete lateral diaphragm. Other details of ileostomy formation are as previously described.[2, 5] A liver biopsy is always taken.

In the first 48 hours after operation, the ileum remains closed.[7] At about 48 hours postoperatively, a No. 16 French soft rubber catheter with 5 or 6 holes is inserted 8 or 10 cm. into the ileum through the center of the ileac end-closure and secured by a purse-string suture of 000 catgut. One-half Wangensteen suction is applied to the catheter, supplemented with 0.9 per cent saline irrigations if cramps occur. Wangensteen nasal gastric suction may usually be removed at 96 hours. At 5 days after surgery, a second catgut purse-string suture is placed 3 or 4 mm. outside the first to avoid late leakage. At 7 days, the ileostomy segment is amputated 1 cm. from the skin. The skin-ileac sutures are removed, and a well-fitting Koenig-Rutzen bag is applied. Measurement for permanent bag is made 3 weeks later.

Colectomy and Ileoproctostomy.—If the rectum is to be left in continuity, the decision as to level of amputation of ileum is as above, and the superior hemorrhoidal vessels are preserved. Whether the anastomosis is made by the open or closed method is immaterial, if bowel preparation is adequate, but no catgut should be employed.[4] In prophylaxis against late cancer development, the anastomosis is made low enough so all the remaining colon may be periodically examined by proctoscopy.

Rationale of Techniques in Operations on the Bowel in Idiopathic Ulcerative Colitis

Requirements of a Good Ileostomy.—Several years ago McKittrick and Miller[14] suggested that the supposed ascending enteritis involving the ileum above the level of ileostomy is usually due to the manufacture of a poor ileostomy at the time of surgery. Two patients have indeed been found in whom ileostomy had been done in conjunction with pancolectomy for polyposis, in whom a clas-

sical clinical picture of ascending enteritis had subsequently developed. In both it was relieved by the performance of a good ileostomy. Further support of this thesis, in regard to the ulcerative process altogether, is found in our observation of 4 patients with cancers of the left colon, in whom pathologic studies showed areas of apparently classical idiopathic ulcerative colitis above the partially obstructing cancers, with no involvement whatsoever below. This has been previously described by Kasich, Weingarten, and Brown.[9] The thesis is also consistent with the observation of Zimmermann[21] that the ulcerative process in the colon often subsides remarkably following sigmoid colostomy.

Table X suggests the part of both technique and proper selection of level of ileum in performance of ileostomy. Complete freedom from complication except excoriation occurred in but 17 of 31 double-barrel ileostomies. The complications besides hernia and prolapse in this group include extensive skin excoriation (5 cases), breakdown of the wound (2 cases), obstruction (1 case), torsion (1 case), and enteritis (1 case).

TABLE X. INFLUENCE OF INVOLVEMENT OF THE ILEUM AT SITE OF ILEOSTOMY AND OF TECHNIQUES USED ON SUCCESS OF ILEOSTOMY

TECHNIQUE	ILEAC INVOLVEMENT	NUMBER OF ILEOSTOMIES	ILEOSTOMIES ENTIRELY FREE OF COMPLICATIONS		LATE HERNIA (PER CENT)	LATE PROLAPSE (PER CENT)
			NO.	PER CENT		
Double barrel	?	31	17	55	32	13
Single barrel*	Yes	19	12	63	10.5	16
Single barrel*	No sections	32	23	72	12.5	3
Single barrel*	Normal	37	28	76	8.1	0

*Technique described in 1945 or as revised in 1949. Only 2 single-barrel buttonhole ileostomies without sutures have been done in the study period—one prolapsed, the other did not.

A review of techniques and results suggests to us that the major factors in ileostomy formation responsible for the development of obstruction are: (1) secondary adhesion formation, (2) the use of too small an opening through the abdominal wall, and (3) contracture of the mucocutaneous junction. Minimal manipulation of the terminal small intestine and primary resection of the colon appear to have eliminated adhesion formation with obstruction, and the use of a 2½ cm. buttonhole incision and of suture anchorage have been associated with no obstruction in the subcutaneous portions of ileostomies. Some contracture at the mucocutaneous junction occurs in less than half the cases, but is easily prevented by having the patient insert an index finger into the ileostomy with each change of the bag until epithelial healing is complete.

Microscopic Control of Level of Ileac Resection.—About 30 per cent of cases of ulcerative colitis are complicated by ileac extension.[2, 13] In view of this, Cattell[1] has recommended sacrifice routinely of an extensive segment of terminal ileum. On the other hand, we have been impressed with the increasing tendency of ileac content to cause excoriation of the skin as one obtains samples from progressively higher levels.

As a means of resecting all of the diseased ileum, but no more, rapid frozen section for the purpose of identifying mucosal and submucosal cellular infiltra-

Fig. 3.

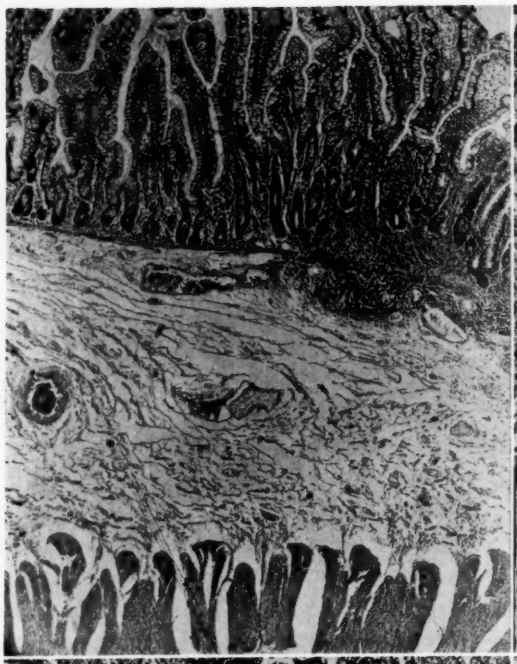

Fig. 4.

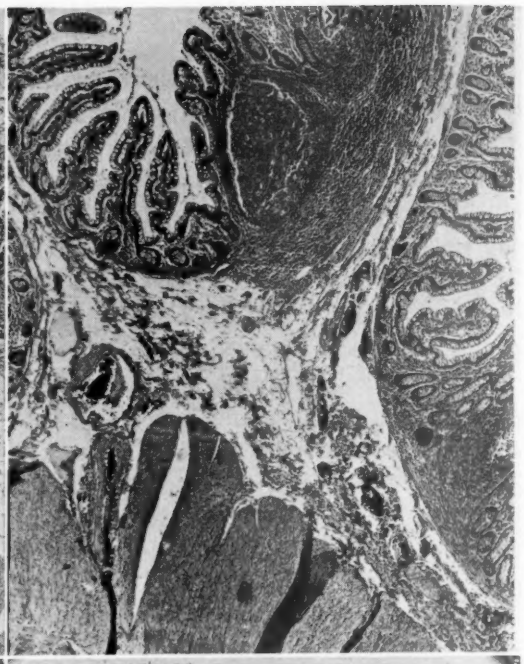

Fig. 5.

Fig. 6

Fig. 3.—Microscopic section of portion of wall of ileum showing very minimal mucosal infiltration with polymorphonuclear and round cells. There is essentially no infiltration of the submucosa by these cells. Paraffin section, hematoxylin and eosin (×30).

Fig. 4.—Microscopic section of portion of wall of ileum showing moderate involvement interpreted as extension of the inflammatory process. There is some necrosis in one of the lymphoid nodules shown. There is rather marked infiltration into the mucous membrane by white cells and there is rather marked infiltration into the submucosa as well. Paraffin section, hematoxylin and eosin (×30).

Fig. 5.—Microscopic section of portion of wall of ileum showing rather heavy involvement interpreted as extension from disease in the colon. There is considerable necrosis in the lymphoid nodule shown. The basement membrane has entirely disappeared in the region of the nodule and there is heavy infiltration, not only out into the mucosa but downward into the submucosa by round cells and polymorphonuclear cells. Paraffin section, hematoxylin and eosin (×30).

Fig. 6.—Microscopic section of portion of wall of ileum from a patient who had suffered from intestinal obstruction without association with idiopathic ulcerative colitis. There is marked edema of the submucosa, but there is no cellular infiltration. Paraffin section, hematoxylin and eosin (×30).

tion has been evaluated by correlation with the subsequent course of the patient. Such microscopic examination has proved to be far more reliable and consistent than gross examination.

Fig. 3 presents the essentially normal picture seen higher in the ileum in these patients. Fig. 4 shows some infiltration by leukocytes both into the mucosa and down into the submucosa. There is frequently at this stage a fair degree of infiltration of the muscularis as well. Fig. 5 is the familiar picture of rather heavy involvement. Fig. 6 presents evidence of edema of the submucosa which was encountered in simple obstruction at an ileostomy which had been improperly made at the time of pancolectomy for polyposis. Here there is no cellular infiltration. When a point in the intestine is reached at which involvement is so minimal as not to be recognizable by the frozen section technique, it has proved satisfactory, in terms of subsequent function, to employ the adjacent segment in the surgical procedure.

This method for determination of level of resection has been employed in 25 cases of ileostomy and 11 cases of ileoproctostomy. Those cases in which the effect of this technique has been specifically sought appear to indicate that the amount of fluid lost from the gut is smaller than if an improper level of ileum is employed. The discharge is also less irritating both to the skin and to the rectum than when a level high in normal intestine or down into involved intestine is chosen. Many ileostomies for which the level has been chosen in this fashion produce formed stool from the time the ileostomy is opened. This stool is usually not irritating to the skin, even on prolonged contact.

Retraction of the ileostomy beneath the general skin surface with each peristaltic action, which renders impossible adequate protection of the skin from the ileac drainage, has complicated 4 ileostomies out of the total group of 119 cases. However, no ileostomy made with ileum of normal microscopic appearance has shown such retraction. Fistula formation also has occurred only in cases shown on such study to have been subjected to ileostomy made with involved bowel. In the 25 cases controlled by frozen section and in twelve others in which routine study of the removed section indicated the ileostomy to have been made just above the upper limit of involvement, there has been but one case of painful skin excoriation. In the other 36 in this group, no skin excoriation whatsoever has been observed.

Suture of Ileum to Anterior Abdominal Wall in Construction of Ileostomy.—Routine examination of the ileostomy from within the abdomen at every opportunity, in the waking state, in the upright and supine positions, on coughing, and with or without a finger in the lumen, had led us to believe that prolapse does not occur unless there is also herniation. Herniation is considered present if there is bulging of the adjacent skin on straining or if there is a peritoneal pocket beside the bowel anterior to the plane of the rectus sheath. The development of hernia or prolapse is related both to employment of involved small intestine and to the manner in which the gut is secured to the posterior rectus sheath and peritoneum. The importance of this latter item is illustrated by the following case history.

The patient was a 32-year-old woman (U. H. No. 651604) with a 10 year history of idiopathic ulcerative colitis and a recent severe flare-up with a pelvic abscess and rectovaginal fistula. On Dec. 20, 1944, a single-barrel ileostomy was performed.[2] The bowel was divided at the upper limit of 40 cm. of grossly involved terminal ileum and the proximal end was used for ileostomy. The mesentery was secured to the anterior abdominal wall with 00 chromic catgut sutures in a caudad direction.

Microscopic examination of the segment of ileum removed showed no ulceration, but the mucosa and submucosa were diffusely infiltrated with plasma cells, eosinophils, and some lymphocytes. Within a few months the patient had developed marked prolapse of the ileostomy, which on one occasion necessitated destruction of her Koenig-Rutzen bag. The patient refused to have further surgery done because of her apparent good health. Because of 2 femoral hernias, she finally consented, and underwent pancolectomy and hernioplasty on Jan. 25, 1946. At this time, it was found that the sutures attaching the ileum to the margins of the buttonhole defect in the abdominal wall had come away from the fascia and the peritoneum, and that the patient had a marked herniation surrounding the ileum. The ileostomy was not disturbed at this time except to place sutures of 0000 silk attaching the bowel wall to the posterior rectus sheath and peritoneum. The mesentery was found still attached as it had been placed at the time of original ileostomy. Gross and microscopic examination of the liver showed portal cirrhosis. Pathologic examination of the colon showed a healing colitis and proctitis, and an area of induration in the sigmoid region 1½ cm. in diameter. Microscopic examination showed adenocarcinoma at this point with metastatic tumor in two nodes adjacent to the bowel.

The patient expired from carcinomatosis on Oct. 2, 1948, deeply jaundiced. Subsequent to her colectomy, she had been able to indulge in normal activities for many months without recurrence of hernia or prolapse of the ileostomy.

This procedure for repair of prolapse has been followed in 4 other ileostomies, each successfully. One must conclude that the placement of sutures securing the ileum to the posterior rectus sheath and peritoneum is the essential step in prophylaxis against both hernia and prolapse rather than attachment of the mesentery to the anterior or lateral abdominal wall.

Lateral Septum Formation in Construction of Ileostomy.—In 6 cases of the 119 shown on Table X, torsion of small intestine about the segment of bowel coming up to the ileostomy has occurred, with strangulating small intestinal obstruction. One of these occurred in a double-barrel ileostomy. There were 2 deaths in this group, and, even if the patient survives, the complication is very serious, for loss of large amounts of small intestine in these individuals is poorly tolerated. To prevent such torsion, a mesenteric diaphragm is constructed lateral to the segment of iluem going up to the abdominal wall.

Management of the Rectum.—The method of closure of rigid rectal stumps previously described[2] has proven successful and free of complication; it is, however, rarely needed now, for the availability of better caloric and antibiotic preparation has made possible the removal of rigid-walled rectums at the initial sitting.

The removal of no more than the rectal wall proper serves to avoid injury to the nervi erigentes and to avoid the leaving of a large dead space in the pelvis. Interview of some dozens of patients after such proctectomy revealed none with loss of sexual function, in sharp contrast to the findings after standard abdominoperineal resection.

Standard wide abdominoperineal resection for patients with colitis has been followed by delayed healing of perineal wounds, late fistulas and abscesses,

and painful scars. By the conservative method, the period of healing has been as short as 3 weeks, and is usually no more than 3 to 4 months, in contrast to 2 to 3 years in a series of such patients proctectomized for ulcerative colitis by the more radical methods used for cancers.

PREPARATION OF THE PATIENT FOR OPERATION IN THE MANAGEMENT OF IDIOPATHIC ULCERATIVE COLITIS

A major item in the successful management of septic or very ill cases in preparation for colectomy is that of nutrition. This is difficult to accomplish when any oral feeding seems to accentuate the loss of protein, salt, and water through diarrhea. It has been found that placement of a long plastic intravenous tube* through the cubital vein into the superior vena cava is of tremendous help.[20] A 15 per cent solution of glucose containing one unit of insulin for each 5 or 6 Gm. of glucose may be run into this tube as a continuous infusion. This method has served, with frequent transfusions, to provide caloric support of the patient (2,000 calories a day) for as long as 19 days (U.H. No. 706087), with but 2 pounds weight loss. Frequent checks of blood sugar level guard against unsuspected hypoglycemia. Rigorous supervision of the administration of sodium, potassium, and chloride is also essential.

The frequency of thrombophlebitis in these cases has led to the complete prohibition of use of the lower extremities for infusion or even for simple venipuncture.

Liberal preoperative employment by mouth of terramycin, streptomycin, and Sulfathaladine seems to have played a large part in reducing risks.

COMMENT

In the selection of patients seen at the University of Minnesota Hospitals, there seems no justification for withholding surgical intervention in most cases of idiopathic ulcerative colitis. Both in terms of survival and in terms of good health, those subjected to surgery have done far better than could have been expected without. Even with limitation of consideration to the complication of cancer alone, this conclusion stands, for the risks of good surgical management are less in this series than those of late malignant degeneration.

Appreciation of the futility of simple excision of involved tissues, in terms of ultimate solution of the problem, has prompted us, and our associates on the medical and surgical staffs, to undertake as careful evaluation as possible of measures directed toward healing of the colon. In this connection, it should be noted that the performance of vagotomy is considered an adjunct to medical therapy by C. J. Watson, who first suggested both vagotomy and pelvic parasympathectomy in this disease.[18] We are all agreed, in addition, that patients who have been vagotomized should be watched critically and subjected to further surgical intervention in case the course is not satisfactory without it.

In a recent paper, Warren and McKittrick report that one-third of their ileostomies required secondary plastic repairs because of stenosis outside the skin.[17] This has not been necessary in the present series. Moderate obstruction

*Obtained from Becton, Dickinson and Company, Rutherford, N. J.

also was a problem to them. In the group we here report, in whom microscopic evidence of normalcy and the desired suture anchorage were both achieved, we have found that roentgenologic or exploratory evidence has shown no enlargement of the ileum just proximal to the ileostomy. We consider such enlargement or hypertrophy, when observed, as evidence of an unsatisfactory ileostomy.

Delay in colectomy is no longer tolerable in the presence of extensive fibrosis, regardless of symptoms, for cancers are then likely to occur, unlikely to be recognized on roentgen examination, and likely to be of high grade.

The patient ill with idiopathic ulcerative colitis tolerates careless or incomplete preparation and makeshift or crude surgery less well than almost any other type of patient. It is essential that his status be precisely evaluated in terms of liver function, salt, water, caloric, and nitrogen balances before any manipulation at all is undertaken, even proctoscopy.

The performance of the surgery proper must be precisely planned and meticulously executed in order to anticipate a smooth and uncomplicated course. In cases in which these precautions are conscientiously observed, it has been possible to accomplish admission to the hospital, preparation for surgery, ileostomy and colectomy, convalescence, and dismissal from the hospital in 10 or 11 days. On the other hand, a single mistake, such as placement of an ileac anchoring suture into the mucosa, or failure to get satisfactory closure of a rectal stump, may lead to a chain of complications terminating in the loss of the patient.

Bitter experience has led us to the conclusion that those patients developing any significant complications following ileostomy, or ileostomy and colectomy, should be placed on anticoagulant therapy regardless of the presence or absence of signs of thrombosis.[3] In a major share of those who die, the terminal event is pulmonary embolus if this precaution is not taken.

CONCLUSIONS

1. At the University of Minnesota Hospitals, those patients with idiopathic ulcerative colitis who were subjected to surgical management were found to do strikingly better than those handled without any surgical intervention. This was true both in terms of survival and of good health. In general the sicker patients received operative treatment.

2. In this series of 267 cases, ileostomy and colectomy proved to be safer than any other method of management of idiopathic ulcerative colitis, including good conservative management. Limitation of University Hospitals admissions to referred cases, however, results in some selection of cases.

3. Idiopathic ulcerative colitis is a precancerous lesion. The frequency of cancerous degeneration apparently increases as the years go by.

4. The risks of ileostomy and colectomy as a one-stage procedure are far lower than the risks of ileostomy alone.*

*After the preparation of this paper, the authors became aware of the work of Charles B. Ripstein, Professor of Surgery at the State University of New York, College of Medicine, at New York City. He and Miller discovered the advantages of primary colectomy independently and almost simultaneously with Wangensteen and Toon. See Miller, Gavin, Ripstein, C. B., and Tabah, E. J.: Surgical Management of Ulcerative Colitis, Surg., Gynec. & Obst. 88:351, 1949.

5. The risks of ileostomy and colectomy as a one-stage procedure for colitis of over 5 years' duration are lower than the risks of developing cancer in the colon.

6. The precise level to which the terminal ileum should be resected is better determined by rapid frozen section than by gross examination.

7. Colitic patients with minimal fibrosis demonstrable roentgenologically or proctoscopically appear definitely to benefit by vagotomy, but longer study is needed for full establishment of the place of this measure and the risk of late cancer.

8. The risks of anastomosis of the ileum to the rectum, with resection of the intervening involved intestine, appear to be higher than the risks of ileostomy and colectomy as a one-stage procedure. If cases are carefully selected for this procedure, however, most of them can be expected to achieve a very satisfactory result.

9. There is no need for loss of sexual function associated with removal of the rectum for uncomplicated idiopathic ulcerative colitis.

10. Arthritic complications of idiopathic ulcerative colitis are usually ameliorated or cured by colectomy.

ADDENDUM

Since submission of this paper for publication, one additional patient has developed carcinoma in a rectum which was preserved and utilized because it appeared normal on proctoscopic examination, and because both rectum and ileum appeared normal on microscopic examination. The time relations are: onset of colitis, 1939; ileostomy, 1946; colectomy and ileoproctostomy, 1947; negative biopsies of polyps, 1950 and 1951. Biopsy of suspicious lesion in 1952 revealed adenocarcinoma. Radical proctectomy, June, 1952, showed no gross evidence of spread.

The authors wish to express their warm appreciation to Dr. O. H. Wangensteen, Chief of the Department of Surgery, for the manner in which he made possible the organization of the care of these patients over these years, for his many valuable and thought-provoking suggestions, for the supervision and care which he provided in a large group of patients included in this report, and for his ever sympathetic understanding in times of trouble. We would like also in particular to express our appreciation to Dr. C. J. Watson, Chief of the Department of Medicine, for ideas, stimulus, and help throughout the study and for his generous part in creating a cordial, cooperative atmosphere in which the welfare of the patient has been the one dominant consideration. We also wish to express our appreciation to Dr. Alan E. Treloar, Professor of Biostatistics, for counsel in evaluation of statistical data, and to Dr. James R. Dawson, Jr., Chairman of the Department of Pathology, for the guidance and help which he provided in connection with microscopic studies.

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Book Reviews

Surgery of Peripheral Nerves. By Emil Seletz, M.D., F.A.C.S., F.I.C.S., Assistant Clinical Professor of Neurological Surgery, University of Southern California School of Medicine, Associate Senior Attending Neurosurgeon, Cedars of Lebanon Hospital, Junior Attending Neurosurgeon, Los Angeles General Hospital, Los Angeles, Calif. Pp. 212, with 136 illustrations. Springfield, Ill., 1951, Charles C Thomas, Publisher. $10.75.

This monograph is an atlas primarily of the anatomy and to a lesser extent of the surgery of peripheral nerves. The value of the book lies in the excellency of the illustrations which include drawings and photographs.

Included in the first chapter is a brief discussion of the proper and improper methods of surgical exposure of nerves, of the various methods of suture, and of the postoperative management of nerve injuries. This is simply a review of known data, but it is very well illustrated and, hence, is of value. The subsequent eighteen chapters are essentially verbal and graphic descriptions of injuries of the peripheral and cranial nerves. Under the discussion of each nerve is given an anatomic description, the character of the symptoms of the lesion in such a nerve, the surgical anatomy thereof, precise methods of exposure, and special procedures that might be adapted to that specific nerve. Here again it is the illustrations that make the monograph of value.

This book is very highly recommended. It is believed to be the most complete and adequately illustrated book in existence on peripheral nerve injuries. It should prove valuable for teaching students as well as for quick reference by physicians encountering patients with nerve injuries and by surgeons specializing in the care of peripheral nerves.

Untoward Reactions of Cortisone and ACTH. By Vincent J. Derbes, M.D., F.A.C.S., Associate Professor of Medicine, Tulane University, Head of Department of Allergy, Ochsner Clinic, Visiting Physician, Charity Hospital, Staff Member, Foundation Hospital, New Orleans, La., and Thomas E. Weiss, M.D., Instructor in Medicine, Tulane University, Member Department of Medicine, Visiting Physician, Charity Hospital, Staff Member, Foundation Hospital, New Orleans, La. Pp. 77, with 2 illustrations. Springfield, Ill., 1951, Charles C Thomas, Publisher. $2.25.

ACTH and cortisone produce widespread effects involving practically every physiologic system which has so far been studied. Although such effects may severely complicate treatment with these substances, it is not strictly proper to refer to them as side reactions since they represent normal actions of naturally occurring endocrine substances. This little volume reviews briefly the physiology of pituitary and adrenal functions and discusses systematically the untoward effects which the materials have been found both clinically and experimentally to exert on various organic functions. These are separately considered in chapters devoted to the glands of internal secretion, electrolytes, cardiovascular system, infections, musculoskeletal system, skin, central nervous system, and gastrointestinal tract.

The volume will be of considerable interest to surgeons who now frequently receive patients for treatment who have been on prolonged ACTH or cortisone therapy and who may be called upon for treatment of such complications as gastrointestinal ulceration or perforation.

Medizinische Röntgentechnik. Vol. I. Skelettaufnahmen und Organuntersuchungen. By Herbert Schoen. Pp. 224, with 476 illustrations. New York, 1951, Grune & Stratton, Inc., Agents for U.S.A. DM22.50.

This is the first of two volumes devoted to radiologic technology. The first volume deals wth roentgenography of the skeleton and of various organs. The second volume deals with physical and technical considerations, including the physical basis for roentgen diagnosis and therapy, with sections on roentgen and general photography.

The major portion of the present volume is concerned with positioning and technical factors involved in roentgenographing the various bones and joints of the body in various positions which best serve to demonstrate anatomicopathologic conditions. Each position is demonstrated by three figures. The first shows the patient in proper position, with a metal rod to indicate the direction of the central beam and at which point the central ray intersects the part undergoing radiography. The second figure shows a skeleton with indications of the parts being shown. The third figure demonstrates the radiograph that is obtained when the position and physical factors indicated are used.

About one-fourth of the volume is dedicated to a discussion of the roentgen examination of blood vessels, soft tissues, foreign bodies, organs of the neck, lungs, heart, abdomen, gastrointestinal tract and urogenital system. Short discussions on special procedures such as pneumoencephalography, myelography and hysterosalpingography are included.

A number of the roentgenograms reproduced in the first part of the book are negative prints, such as are usual in American books; in the remainder of the book the roentgenograms reproduced are positive prints, more commonly used in European and other countries. While some may be slightly confused by the transition, it must be stated that the reproductions are clearly printed on good paper.

The present volume is a valuable contribution to the field of medical radiographic technique and, as such, should find a place in the libary of those interested who are familiar with the German language.

Medizinische Röntgentechnik. Vol. II. Edited by Herbert Schoen, with contributions by Erich Bunde and Viktor Loeck. Pp. 328, with 217 illustrations. New York, 1952, Grune & Stratton, Inc., Agents for U.S.A. DM27.

The first volume has been reviewed. This, the second volume, is further divided into two principal sections, one on the physical and technical basis of roentgen diagnosis and therapy, followed by a section on roentgen and color photography.

The first section is a well-coordinated presentation of physical and technical principles. Chapters on fundamentals of electricity, atomic physics, nature and characteristics of roentgen rays, factors in film production, radioactivity, and dosage measurement and protection are included.

The second section is further subdivided into roentgen photography, color photography, and formulas and tables of reagents used in film processing. Basic principles of roentgen photography, materials used, film processing, sources of error and film defects, and many other items of interest are discussed.

It is difficult to review adequately a work of this type in a brief manner, leaving the alternative of merely attempting to explain what is included and the manner of developing the organized presentation. Suffice it to say that in editing this two-volume set on medical roentgen technique, Professor Schoen has given to the medical world a unique combination of radiophysics, film production and processing, and technique of positioning which is seldom seen as a unit work, and which, as such, should be of considerable value.

Lehrbuch der Röntgendiagnostik. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. Vol. I, Section 5, Innere Organe. Pp. 436, with 522 illustrations. New York, 1951, Grune & Stratton, Inc., Agents in U. S. A. DM 84.

The previous sections published to date have been reviewed in earlier issues of the journal. This comprehensive review of the field of diagnostic roentgenology is being published in paper-bound sections which later may be bound into more permanent volumes. An English edition is also being prepared.

This section is the first on internal organs and, specifically, represents the first portion of the volume on the thorax. Considerable space is devoted to the normal thorax, considering various anatomic and physiologic features involved in fluoroscopy and roentgenography.

Diseases of the trachea and bronchi are given full consideration. Diseases of the lungs properly begin with consideration of emphysema, atelectasis, and circulatory changes. Accounts of inhalation and various dusts (pneumoconiosis) and of various chemical irritants, lobar pneumonia and various forms of bronchopneumonia or segmental pneumonia follow in succession. Over 100 pages are devoted to the pathogenesis and roentgen picture in various stages and forms of pulmonary tuberculosis.

As in the previous sections the high quality of text and reproductions is maintained. It seems safe to predict that the completed work will represent the most exhaustive general survey of diagnostic roentgenology yet published. The English translation will be of great value to those who do not read German.

Lehrbuch der Röntgendiagnostik. By H. R. Schinz, W. E. Baensch, E. Friedl, E. Mehlinger, with several contributors. Ed. 5. Section 6: pp. 544, with 507 illustrations, 10 tables. DM 98. Section 7: pp. 453, with 516 illustrations. DM 89. New York, 1952, Grune & Stratton, Inc., Agents for U. S. A.

As stated in previous reviews, this voluminous text on diagnostic roentgenology is appearing in successive paper-bound sections, which may, in turn, be bound as permanent volumes when the work is complete. The first four sections constitute Volumes I and II, covering the discussion of the skeleton. Volume III concerns internal organs, and Section 5, reviewed previously, contains most of the material on the lungs.

Section 6 completes the study of the lungs, and proceeds to elucidate upon the pleura, diaphragm, mediastinum, heart and blood vessels. A rather complete roentgen analysis of pulmonary tumors, benign and malignant, is given. More uncommon pulmonary diseases, including mycoses, parasitic infestations, pulmonary fibrosis, pulmonary ossification and amyloidosis are briefly discussed. The pleura, diaphragm, and mediastinum are amply discussed, followed by tables and sketches illustrating differential diagnostic features in diseases of the lungs, pleura, diaphragm, and mediastinum. The portion dealing with the heart and great vessels is quite ample, including necessary information on congenital heart disease, and presenting valuable aid given by angiocardiography, cardiac catheterization, and kymography.

Section 7 continues with diseases of the aorta. Brief coverage is given to the coronary vessels, other great vessels, and peripheral vessels. This is followed by tables and sketches summarizing congenital and other cardiovascular lesions. A chapter is devoted to developmental aspects of pulmonary and cardiovascular diseases.

This section also includes a major portion of the gastrointestinal tract. Use of contrast media and methods of depicting lesions in various portions of the digestive system are presented. Diseases affecting the mouth, pharynx, esophagus, stomach, duodenum, small bowel, and appendix are described and illustrated clearly.

Up to this point, the authors have certainly fulfilled the prediction that this total work would represent an outstanding system of diagnostic roentgenology. The earlier parts have appeared in the English translation and the remainder will be eagerly awaited by those who are not familiar with the German language.

Die Entzündungsbestrahlung. By Habil R. Glauner, M.D., Associate Professor of Radiology and Director of Roentgenology, Marien Hospital, Stuttgart, Germany. Ed. 2. Pp. 189, with 13 illustrations. Stuttgart, 1951, Georg Thieme. $4.45.

The success of chemotherapy and antibiotics has reduced the usefulness of radiation in combating infections. The author is, however, convinced that many inflammatory conditions still respond better to roentgen irradiation than to any other known therapy. He emphasizes the local effect of irradiation and limits its use mainly to infections which are walled off by tissue reactions such as edema, leukocytic infiltration, and, finally, connective tissue formation preventing a satisfactory concentration of antibiotics.

It is a carefully written and well-authenticated book. The first half (the General Part) is devoted to the nature of inflammation and the action of radiation. Numerous studies and experiments are cited. It ends with nineteen statements which represent the author's theory concerning the action of radiation on inflammatory processes and gives indications and contraindications for the use of radiation therapy. This part has not been changed considerably from the first edition published in 1940.

The second part (the Special Part) discusses in detail the different groups of infections which, according to the author, usually respond well to irradiation.

Among dermal infections are mentioned in particular, furuncles and carbuncles, and subdermal infections include abscesses and phlegmons which may be irradiated either before or after surgical incision, while some may resolve without incision. Of particular interest is the discussion of hydradenitis which is the only type of infection requiring relatively high doses.

The next chapter discusses treatment of lymphangitis and inflammation of lymph nodes. The author then considers secretory organs. He considers roentgen therapy the method of choice for puerperal mastitis, and in discussing salivary glands, emphasizes that he has obtained good results with irradiation of postoperative parotitis.

Another chapter is devoted to inflammations in the oral cavity. It includes a very extensive discussion of the irradiation of the tonsils. The author emphasizes that the present-day aim of the treatment is mainly to reduce recurrent acute tonsillitis and pharyngitis and, incidentally, to shrink the tonsils and surrounding lymphatic tissue. Many reports are cited. Inflammations of the teeth and their surroundings are also considered an indication for irradiation, and the author reports interesting results both in regard to healing and pain relief.

It is not my intention to report all the chapters here or all the types of inflammations included in the book. Only the more extensive or important ones are mentioned, and among these must be included the inflammations of bones and joints. Radiation is not indicated for osteomyelitis, but the author advises the use of a rather extensive series of exposures for panaritium ossale (felon with necrosis of distal phalanx) which may result in regeneration and thus prevent the necessity of amputation. The author does not favor irradiation for polyarthritis rheumatica, but is emphatic about its value for pain relief in "deforming joint diseases." He discusses in considerable detail the treatments and the results obtained, and refers to von Pannewitz's publication in 1933 as fundamental.

The last chapter deals with tuberculosis and especially the value of irradiation for cervical adenitis and female genital or pelvic involvement. Tuberculosis of the eye, and particularly of the larynx, is stressed with the understanding that antibiotics may to a certain extent replace or supplant x-ray therapy.

A brief summary of indications and contraindications completes the discussion, followed by an extensive list of references (189 pages).

The different problems are carefully considered, and the book is a valuable contribution to the consideration of x-ray treatments for inflammatory conditions. It is particularly recommended for radiologists, who ought to become familiar with the viewpoints advanced by the author.

Totale Cystektomie beim Blasenkrebs. By Prof. Dr. Hans Boeminghaus. Pp. 84, with 56 illustrations. Paper bound. Stuttgart, 1951, Georg Thieme. DM 11.50.

This is a systematic review of the subject of diversion of the urine and cystectomy for neoplasms. The author points out that the mortality of this procedure has been so high for so long that many surgeons have come to regard it as hopeless. He has apparently been led to review the subject by his experience with fourteen consecutive cases without an operative death. He attributes the current decline of surgical mortality to improvements in surgical technique, to the availability of antibiotics, and to the use of transfusion: The mortality rate has fallen from its original level of 65 to 75 per cent to somewhere between 8 and 15 per cent in the more recent literature.

There are brief discussions of the frequency, location, types and degree of malignancy, depth of infiltration, and metastasis of carcinoma of the bladder. Other methods of treatment are reviewed. Boeminghaus is discouraged with the results of x-irradiation, and has had no experience with radium nor with radioactive isotopes. He employs cystoscopic operations for noninfiltrating neoplasms, but condemns such methods, as well as suprapubic diathermy and segmental resection for infiltrating tumors, saying that the presence of nests of malignant cells at a distance from the primary tumor defeats their use. Such palliative operations as diversion of the urine, excision of the presacral and pelvic nerves, and the subarachnoid injection of alcohol are mentioned.

Boeminghaus feels that no precise indications for cystectomy can be established. In his opinion the two principal indications for its use are infiltrating tumors without extravesical extension, and papillomatosis that cannot be controlled by other methods. Contraindications include advanced years, poor general condition, severe damage to the upper urinary tract, and local fixation or metastasis. He agrees with Jewett that the best guide to local operability is bimanual palpation under anesthesia: Large hard masses and fixation mean that the lesion is inoperable.

The discussion of technique is fairly detailed. Methods of diverting the urine depend upon the condition of the upper urinary tract. If both sides are normal he favors bilateral ureterosigmoidostomy; if only one kidney is normal, its ureter is implanted into the bowel, while the other is dealt with by temporary nephrostomy and later ureterosigmoidostomy or nephrectomy. Bilateral damage may require cutaneous ureterostomy, which may occasionally be followed by ureterosigmoidostomy if the kidneys improve, an event quite unlikely to occur. In general he seems to favor bilateral ureterosigmoidostomy followed later by abdominal cystectomy.

Patients are prepared for ureterosigmoidostomy, as in this country, by catharsis, enemas, low residue diets, and oral antibiotics, of which he prefers Aureomycin. The anastomosis is performed sometimes through bilateral inguinal incisions with extraperitoneal exposure of the ureter, the parietal peritoneum being sutured to the sigmoid so that the anastomosis is extraperitoneal as advocated by Cabot and by Priestley; at other times it is performed through a median transperitoneal incision, the details being similar to those described by Dodson. Boeminghaus, however, leads the ureter into the lumen of the sigmoid with a catgut suture which transfixes the end of the ureter and passes through a small stab in the bowel. The ureter is anchored to the colon with three fine sutures in the adventitia, and the whole thickness of the wall of the sigmoid is formed into a tunnel around the ureter by Lembert sutures.

He describes simple cystectomy, radical cystectomy, and sacral, vaginal, abdominal, and combined methods. The presentations of technique are well illustrated. Fourteen cases are reported, nine of them two-stage abdominal, and five of them single-stage sacral, operations. His discussion of results is based upon the literature. That they are very poor is attributed to the carcinoma itself, overlooking the obvious fact that many failures are due to the adverse effects upon the kidneys of exposing them to the infected contents of the colon. Complications such as pyelonephritis and hyperchloremic acidosis are not mentioned. This work is useful (to those who read German) as a fairly detailed review of the subject.

Topographische Ausdeutung der Bronchien im Röntgenbild. By Priv.-Doz. Dr. Claus Esser. Pp. 152, with 77 illustrations. Stuttgart, 1951, Georg Thieme. DM 33.

This monograph, written by a roentgenologist of the Johannes Gutenberg University, Mainz, fulfills definite needs in medical literature. Specifically, there is comparison and correlation of the various systems of nomenclature of the segmental branches of the bronchial tree, and there is correlation of the anatomic structure of the bronchi with their appearance in the bronchogram in various positions.

After preliminary discussion of the historical features and practical uses of knowledge of bronchial anatomy, there follows a general discussion on development, anatomy, nomenclature, and segmental vasculature of the lungs. Roentgen examination of the bronchi is briefly described.

In the section on special topography of the bronchial tree a systematic approach is used. Each lobe of the right and left lungs is described in sequence. In each instance the various systems of nomenclature are tabulated, anatomic sketches are shown, segmental vessels and variations listed, and well-selected bronchograms illustrate the bronchial picture described.

This is a thorough résumé of bronchial and bronchographic anatomy and as such should prove of value to roentgenologists, chest physicians, surgeons, and all those interested in the anatomy, diagnosis, and treatment of the chest.

Leitfaden der Laparoskopie und Gastroskopie. By H. Kalk, W. Bruhl, and W. Burgmann. Pp. 158. Stuttgart, 1951, Georg Thieme. DM 27.

This small manual deals with two important diagnostic techniques, namely, peritoneoscopy and gastroscopy. It is concisely written and beautifully illustrated. Kalk and Burgmann describe the apparatus employed for laparoscopy (peritoneoscopy) and liver biopsy. The extensive experience of the senior author in this field is apparent from the practical suggestions on technique that are included. The illustrations (sketches, diagrams, and photographs) enable the reader to follow the directions with such ease that a limited ability to translate German should prove to be no great handicap.

Kalk has employed peritoneoscopy extensively in the diagnosis of liver disease and a large section of the monograph deals with the findings one encounters in various types of hepatic pathology. The drawings, by Max Landsberg, depict a variety of abnormalities that may be visualized through the peritoneoscope. These are produced in excellent color and add much to the value of this book.

The authors cite many valid reasons for favoring the employment of "guided" needle biopsy of the liver by this method, i.e., under visual control during peritoneoscopy. It seems unlikely, however, that clinicians in the United States will be dissuaded from the current practice of needle biopsy of the liver as it is customarily performed at the patient's bedside (the so-called "blind puncture" method). The simplicity of the latter is a decided advantage and, at least in this reviewer's experience, is accompanied by less discomfort for the patient. No one will deny the value of direct visualization of the liver; the characteristic changes seen at peritoneoscopy often permits an immediate diagnosis (for example, coarsely nodular cirrhosis, metastatic carcinoma, and so forth) without resort to biopsy.

The section on gastroscopy has been written by W. Bruhl. This, too, is concise, well illustrated, and can be translated without difficulty even if one's reading knowledge of German has diminished through disuse.

This manual can be highly recommended to anyone contemplating the use of peritoneoscopy or gastroscopy. The endoscopist, already familiar with these methods, will find much information that will be of value to him.

Surgery of the Oblique Muscles of the Eye. By Walter H. Fink, M.D. Pp. 350 with 93 illustrations, 18 in color. St. Louis, 1951, The C. V. Mosby Co. $8.75.

The author has written and assembled a thorough work on the oblique muscles. The anatomic portion is well covered and extremely well illustrated. The illustrations consist of drawings and photographs showing anatomic dissections in great detail.

The physiology is adequately covered. The surgical indications are well presented with excellent recommendations as to surgery and magnificently illustrated surgical techniques.

This volume is a highly specialized one and probably would hold little interest for the general surgeon. It should be of great help to the ophthalmic surgeon.

Causalgia. By Frank H. Mayfield, M.D., Assistant Professor of Clinical Surgery, College of Medicine, University of Cincinnati, Attending Neurological Surgeon, Bethesda Hospital, Christ Hospital, Deaconess Hospital, Good Samaritan Hospital, St. Francis Hospital, and Jewish Hospital, Cincinnati, Ohio. Pp. 65, with few illustrations. Springfield, Ill., 1951, Charles C Thomas, Publisher. $2.25.

Causalgia is a severe, burning pain in an extremity after injury to a peripheral nerve. Vasomotor and trophic changes are usually present, and the condition is relieved by interruption of the sympathetic nerves. This monograph presents a brief historical introduction, followed by data from 105 cases of true causalgia seen by the author in military service. In each patient, the original lesion was an incomplete, penetrating wound of a large peripheral nerve, usually the median or sciatic. Symptomatology and the clinical course are described in detail. The techniques of sympathectomy are illustrated. The book concludes with a discussion of theories about the causative mechanism.

Die Krankheiten der Nasennebenhöhlen, der Ohren und des Halses im Röntgenbild. By Prof. Dr. Richard Mittermaier, Director of the University Ear, Nose and Throat Clinic, Marburg/Lahn. Ed. 2. Pp. 232, with 483 illustrations and reproductions. DM 66. New York, 1952, Grune & Stratton, Agents for U. S. A.

This enlarged second edition consists of five parts. The first part is an introduction in which roentgen apparatus, technique, and general anatomic and pathologic data concerning the paranasal sinuses, temporal bone, mouth, larynx, and throat are briefly discussed. The subsequent four parts are in atlas style, presenting the same anatomic divisions.

A flexible apparatus such as that designed by Lysholm for skull roentgenography is desirable. Roentgenography of the paranasal sinuses should be done with the head upright, thus aiding in demonstrating air-fluid levels. Use of a grid is desirable in fairly large films such as are used for the paranasal sinuses, in order to cut down secondary irradiation. This is not of as great importance when smaller dimensions are involved, such as are used in studying the mastoids. The small-focus tube should be of great value. Rays of only moderate penetration should be used to better portray soft tissue changes. Stereoscopic pairs are of value in aiding anatomic orientation and in studying fractures and location of foreign bodies. Proper positioning is essential to demonstrate anatomic and pathologic features.

In the atlas portions each part begins by demonstrating positions, and correlating normal roentgenograms with labelled anatomic sketches. This is followed by reproductions of roentgenograms showing pathologic changes with legends discussing pertinent clinical data and interpretation of the roentgenograms.

As is usual in continental books, the roentgenographic reproductions are positive. Details are clear and soft-tissue changes are adequately portrayed. This atlas is useful in demonstrating basic fundamentals to the student and should serve as a reference for the experienced radiologist.

The Thyroid. By Thomas Hodge McGavack, M.D., F.A.C.P., Professor of Clinical Medicine, New York Medical College, Director of the New York Medical College Metropolitan Hospital Research Unit. With a section on Surgery by James M. Winfield, M.D., F.A.C.S., Professor and Director of Surgery, New York Medical College; and Walter L. Mersheimer, M.D., F.A.C.S., Associate Professor of Surgery, New York Medical College; and a section on History in collaboration with Dorothy B. Spear, Ph.B. Pp. 646, with 72 illustrations in black and white. St. Louis, 1951, The C. V. Mosby Co., $13.50.

In the preface, the author states that the major effort of the volume has been directed toward a summary of the more important contributions in recent years concerning the thyroid gland, an indication of the author's preference concerning many questions still in dispute, and a rationalization of some of the chemical and physiologic aspects of the thyroid in order to make them available to internists as well as to the investigator and student.

The book is organized into forty-six chapters, consisting of separate topics. A short section on the historical aspects of anatomic, physiologic, and surgical discoveries concerning the thyroid gland are included.

The sections on the anatomic and embryologic considerations of the thyroid gland, as well as the section on the surgical anatomy of the thyroid gland, are not illustrated. Similiarly, the sections concerned with the pathology of the thyroid gland do not contain either illustrations of gross specimens or representative photomicrographs.

The chapter dealing with the relationship of the thiocyanates, antithyroid agents, and iodine to thyroid physiology is excellent. Simple line graphs are used to point out the pertinent factors without oversimplifying the physiology involved. There is also an adequate description of the more recent research activities involving the use of radioactive tracers.

A section entitled "Heterotrophic Thyroid Tissue" includes such clinically significant anomalies as the lingual, sublingual, and prelaryngeal thyroid and the so-called "lateral aberrant thyroid" syndrome. The author states that the latter topic was placed in this section in order to emphasize its importance! Both the older concept that lateral aberrant thyroids were developmental anomalies and the more recently accepted concept that lateral aberrant thyroids are indeed metastatic thyroid tumors are presented.

This book can be recommended as a textbook on the thyroid for internists and medical students.

Einführung in die Röntgenologie. By G. F. Haenisch, H. Holthusen, and A. Liechti. Ed. 5. Pp. 521, with 371 illustrations. Stuttgart, 1951, Georg Thieme. DM 60.

This standard German textbook has been completely revised and expanded. As in previous editions, there is a relatively small section of forty-five pages devoted to physics and technique, followed by larger general sections on roentgen diagnosis and therapy.

The section on diagnostic roentgenology not only has been completely revised in the individual components, but also has been considerably expanded to cover new developments since previous editions. Use of roentgen methods in studying anatomy and physiology of bones, respiratory and circulatory systems, as well as of the gastrointestinal tract is discussed. The portion on the biliary system is expanded to include cholangiography. More attention is also devoted to the studies of peripheral vessels and diseases of women, indicating the more recent developments in these fields.

The section on therapy also has been enlarged and includes use of radium, radon, contact, supervoltage, and rotation therapy.

Altogether this new fifth edition comprises a good general survey of the field of radiology and as such will continue to serve as a useful text for the student and physician desiring a thorough yet concise reference.

Chloroform, A Study After 100 Years. Edited by Ralph M. Waters, M.D., retired Professor of Anesthesiology and Head of the Department of Anesthesia, University of Wisconsin College of Medicine, Madison, Wisconsin. Pp. 138. $2.75. Cloth. Madison, 1951, University of Wisconsin Press.

This book is of particular interest to the anesthesiologist. It represents a modern clinical and laboratory evaluation of the "ancient" and discredited anesthetic agent, chloroform. Through meticulous attention to the fundamental physiologic principles of respiration and by refinements in the technique of administration, this potent and "lethal" agent was administered to over 1,000 cases. The anesthetic mortality and morbidity rates did not incline as one would have predicted. All in all, chloroform was used in every type of operation and on all classes of anesthetic risks, with relatively no impairment in hepatic, renal, and cardiac function.

This monograph emulates the spirit and leadership of Dr. Waters in that it depicts a decade of interdepartmental cooperation and teamwork. The Departments of Pharmacology, Pathology, Biostatistics, Internal Medicine, Surgery, and Anesthesiology contributed equally to the laboratory and clinical data and to the actual writing of the manuscript. Dr. Waters not only initiated and directed the project, but also contributed to much of the clinical work. Above all, he was the constant liaison between all of the previously mentioned departments.

Although the clinical and laboratory findings tend to place chloroform in a new and safer scale, Dr. Waters does not hesitate to emphasize that the agent was administered by individuals acutely aware of its dangers and capable of skillfully providing ideal physiologic conditions. Their constant maintenance of adequate oxygenation and reliable control of the anesthetic vapor tension contributed to the success of these studies. Chloroform will continue to be a hazardous anesthetic until a foolproof method is perfected for recording and controlling its inspired vapor tension.

Die zerebrale Angiographie. By H. Krayenbuhl, Professor of Neurosurgery, Director of Neurosurgical Clinic, University of Zurich, and H. R. Richter, Assistant, Neurosurgical Clinic, University of Zurich. Pp. 217, with 100 illustrations. Stuttgart, 1952, Georg Thieme. DM 59.70.

Highly recommended is this very instructive atlas on cerebral angiography. It is prepared on unusually fine grade paper so that the illustrations, which are both photographs and freehand drawings, are clearly delineated. The description of technique and interpretation of the radiographs, though concise, are thorough.

The book is divided into three principal parts. The first is a short historical review of angiography and a description of the various techniques used in carotid and vertebral angiography. It includes the positioning of the patient, anesthesia of choice, method of puncture, and postangiography care. Unfortunately there is very little included on complications. The second part concerns the anatomy and physiology of the cerebral vascular system. Both normal and variations of normal angiograms are illustrated in adequate detail. This is a valuable section. The section on physiology is very brief and includes only the barest fundamentals of the intracranial blood flow. The third part, which is subdivided into two sections, comprises the major portion of the book. The first subdivision is a description of the angiographic appearance of the congenital and acquired vascular lesions, of methods of localization and histologic diagnosis of neoplasms, and of the recognition of hydrocephalus and subdural hematomas. The second subdivision consists of a series of clinical reports taken from the author's clinic. The clinical data are given in detail and the angiograms have been excellently reproduced. Usually there is an accompanying freehand drawing to assist the reader in the interpretation. Each case can and should be read in detail to understand the author's sequence of therapy and interpretation of the angiogram. This section is the highlight of the book; it is excellent.

A comprehensive bibliography is furnished at the end of the book.

Anatomy in Surgery. By Philip Thorek, M.D., F.A.C.S., F.I.C.S., Assistant Clinical Professor of Surgery, University of Illinois College of Medicine, Chicago, Ill. Pp. 970, with 720 illustrations by Carl T. Lindey. Cloth. Philadelphia, J. B. Lippincott, $22.50.

For several reasons this is an excellent volume for any surgeon to own. More than likely many medical students also will find it a useful volume.

The illustrations are abundant and unusually good. Many are in color and we hope that in future volumes this number of color illustrations can be increased. An unusual feature of this volume, which has often been neglected in work of this type, is the large, easy-to-read type for all captions in the illustrations.

Dr. Thorek deserves commendation for his lucid, readable style in the text, together with an organization of the material in such a fashion as to make its retention less difficult for the average reader. It is welcome also to find that much verbiage and detailed nomenclature, unessential to the surgeon at least, has been omitted.

The coverage of surgical operations for the most part is good and well integrated with the text on anatomy. A few criticisms might be offered in the hope that the author may care to remedy them in future editions. Namely, the coverage of anatomy and description of the surgery of acquired and congenital heart disease is quite brief. The same may be said for the section on inguinal hernia. A more complete description of some of the standard operations widely used for congenital and acquired heart disease, as well as for inguinal herniorrhaphy, would increase the value of these sections considerably.

All in all, however, as stated before, this is an excellent volume and one which students of surgery of any age or proficiency should find valuable to own.

The Metabolic Response to Surgery. By F. D. Moore, M.D., Moseley Professor of Surgery, Harvard Medical School, Surgeon-in-Chief, Peter Bent Brigham Hospital, Boston, Mass., and Margaret R. Ball, A.B., Department of Surgery, Harvard Medical School, Laboratory for Surgical Research, Peter Bent Brigham Hospital, Boston, Mass. Pp. 153, with few illustrations. Springfield, Ill., 1952, Charles C Thomas, Publisher. $7.50.

This very unusual book, comprising an exposition of present knowledge of the metabolic alterations accompanying surgery, is built around the cases which the authors have intensively studied by metabolic balance methods. The presentation of these cases, supplemented by reference to similarly studied cases which have been reported by other investigators, serves to illustrate the major facts which have been learned concerning the alterations in organic and inorganic metabolism which characterize the patient undergoing surgery.

By suitable experiments it has been possible to isolate the various components of the whole surgical experience and thus to describe the effects of such separate factors as starvation and nutrition, parenteral therapy, the magnitude of the surgical procedure, and the reactivity of the endocrine system. An immense amount of data is included in the form balance charts and tables. The charts, however, are drawn with unusual clarity and are so well correlated with the text that the book can be read without the effort which is frequently required for adequate comprehension of metabolic studies.

This is no practical guide, but a fundamental book. It should be of great interest to surgeons who are interested in the nature of current research in surgical physiology as well as to investigators and to the student who will find it an unusually lucid introduction to the theory and technique of metabolic methods.